CONFORMATION ANALYSIS OF SOME CYCLIC COMPOUNDS BY MOLECULAR MECHANICS AND X-RAY DIFFRACTION

A Thesis presented for

the degree of Doctor of Philosophy

in the

Faculty of Science

of the

University of Glasgow

by

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June 1976

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ACKNOWLEDGEMENTS

I wish to thank the University of Glasgow for providing financial support to enable me to undertake the research for this thesis.

I am indebted to Professor G. A. Sim for allowing me to use the facilities in his department and for much helpful advice and encouragement. To Dr. D. N. J. White I am especially grateful for instruction in the techniques of x-ray crystallography and molecular mechanics and for the manner in which he has constantly strived to improve my understanding of the problems which have arisen.

I must also express my most sincere thanks for the assistance given to me by the staff of the chemistry and computing departments who are too numerous for proper acknowledgement. Particular mention is due to Drs. Gilmore, MacNicol, and Mallinson for their constant and consistent willingness to discuss difficulties.

Finally, I must thank my wife without whose help and encouragement I could not have completed this project.

Glasgow 1976 M. H. P. Guy

ERRATA

Page	Line	
15	22	Delete "of the structure invariants". Insert "arising from the Σ_1 relationships".
17	4	Delete "second Fourier synthesis". Insert "structure factor calculation".
62	16	Add footnote "$ For the Σ_1 relationships only".
98	25	Insert "approximate" before "$\underline{C_2}$".
138	7	Add footnote "$ For the Σ_1 relationships only".
322	8	Insert "energy" after "minimum".

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SUMMARY

This thesis is composed of two parts. In part I the x-ray structural analyses of two sesquiterpenoids and two derivatives of 2-naphthol are reported, while in part II the results from molecular mechanics calculations are used to investigate the conformational processes occurring in a series of cyclo-octa-1,5-dienes and to interpret some of the stereochemical peculiarities of germacrane based sesquiterpenoids.

The crystal structure analysis of the germacranolide, costunolide, was undertaken to determine its structure and stereochemistry. An incomplete structure was available at the commencement of this study, derived partially from x-ray diffraction measurements using Mo - Kα radiation and partially from synthetic and spectral observations. The diffraction data were recollected using Cu - Kα radiation in order to obtain more accurate measurements of the weaker reflexions. This technique was completely successful and allowed the structure and stereochemistry to be determined.

Crystals of the guianolide, mikanokryptin, were supplied by Professor W. Hertz who, on the basis of UV, IR, and NMR spectra, had elucidated most of the stereochemistry. The configurations at C(1), C(6), and C(10) remained uncertain and the x-ray analysis removed the ambiguities at these chiral atoms. In addition, molecular mechanics calculations were carried out for the isolated 1-methylidene-cycloheptane system of mikanokryptin and these allowed observations to be made pertaining to the stereochemistry of this and other guianolides.

Structure analyses of 1-methyl- and 1-isopropyl-2-naphthyl acetate were carried out as part of a series of

investigations, by Dr. J. Carnduff, into the autoxidation of 2-naphthols. It was anticipated that the isopropyl derivative would have been substantially more strained than the 1-methyl compound because of differences in the rates of autoxidation of the corresponding 2-naphthols. The observed structures did not support this view.

Molecular mechanics calculations for syn-3,7-dibromo-cis, cis-cyclo-octa-1,5-diene found the twist-boat conformation as the global minimum, the geometry of which was very similar to that found in an earlier x-ray analysis. The complete pseudorotational cycle was also investigated using this technique. A similar study was carried out for the anti-3,7-dibromo isomer. The conformational processes in the parent diene, cis,cis-cyclo-octa-1,5-diene, were the subject of a variable temperature NMR investigation by Professor F. A. L. Anet and molecular mechanics calculations were used to interpret these spectra and to reproduce the minimum energy geometry found by electron diffraction measurements. The anti-3,7-dimethyl derivative has recently been synthesized by Professor P. Heimbach. He kindly supplied a sample of his product for variable temperature NMR analysis and molecular mechanics calculations have been performed with a view to interpreting the spectra.

The final chapter reports a series of calculations on the stereochemistry of germacranolides. The force field used was able to reproduce the geometry of costunolide,which had been the subject of an x-ray analysis described earlier in this thesis. Subsequent calculations on the two frequently occurring conformations of the cyclodecadiene system in germacranolides have been used to investigate the stabilities of the various modes of

lactone-cyclodecadiene fusion apparent in these sesquiterpenoids and to correlate the conformation of the lactone function with both the fusion and the Cotton effect at 260nm.

PART I

X-RAY DIFFRACTION

CHAPTER ONE

Some aspects of crystallography

1.1 Historical

Modern crystallography is based on the suggestion made by Max von Laue (1912) that the regularly spaced repeating units of a crystal might act as a three-dimensional grating for x-rays. Following the experimental verification of this hypothesis by Friedrich and Knipping, the use of monochromatic radiation and the advent and improvement of the rotating crystal method made it possible to both index and measure the intensity of individual reflexions. The subsequent development of crystallography has been concerned with the sophistication of these basic techniques and the solution of the phase problem.

The phase problem arose because of our inability to refract x-rays and thus obtain an image of the molecular structure.

The phase amplitudes can be derived fairly easily from the intensities but mathematical reproduction of the image required information about the phases. From 1930 onwards a great deal of effort was spent on this task and solutions applicable to certain limited situations were found, but no general approach has been available until recent years.

For many compounds it is now possible to derive the phase relationships directly from the intensity data using a combination of inequality and statistical methods.

The remainder of this chapter is devoted to a more detailed discussion of the specific techniques which have been used in the structure analysis of the compounds which form the subject of the x-ray crystallographic

section of this thesis.

1.2 Corrections to the measured intensities

(a) Lorentz - Polarisation

Lorentz

The time required for a reciprocal lattice point to pass through the sphere of reflexion is not constant but depends on both the Bragg angle and the method of data collection.

For the four circle diffractometer with normal beam geometry the Lorentz factor, **L**, is given by:

$$\mathbf{L} = 1/\sin 2\theta \qquad (1)$$

Polarisation

Partial polarisation of the x-ray beam occurs on reflexion and hence the intensity of the reflected beam is corrected by a factor, **p**, where:

$$p = \tfrac{1}{2}(1+\cos^2 2\theta) \qquad (2)$$

A more complex expression is used when the incident beam is itself partially polarised.

The combined factor, **Lp**, for a four circle diffractometer is therefore:

$$Lp = \frac{1+\cos^2 2\theta}{2\sin 2\theta} \qquad (3)$$

(b) Counting Loss

Automatic data collection instruments use scintillation or proportional counters to measure intensities. When very strong reflexions are present these devices become overloaded and underestimate the true count. One method of overcoming this is to remeasure the low order reflexions at reduced beam intensity and thus obtain a conversion factor for the weaker reflexions which may then be applied to the intense reflexions.

The two intensities for each reflexion may be considered to be related by the following expression:

$$J = P_1 I + P_2 I^2 \qquad (4)$$

where J = intensity at reduced setting

I = intensity at normal setting

and P_1, P_2 are constants to be determined.

Each measurement of J has a standard deviation σJ and can be assigned a weight W, such that:

$$W = 1/(\sigma J)^2$$

The difference Δ between the counts for a given reflexion under the two sets of conditions is:

$$\Delta = J - (P_1 I + P_2 I^2) \qquad (5)$$

and if $M = \Sigma\, W \Delta^2$ then the stationary value of M occurs when:

$$\frac{\delta M}{\delta P_1} = \frac{\delta M}{\delta P_2} = 0 \qquad (6)$$

Thus differentation of equation (5) with respect to P_1 and then P_2 yields two simultaneous equations which can

be solved for the conditions set by equation (6) to yield $\underline{P}_1$ and $\underline{P}_2$. Resubstitution of these constants in equation (5) with the appropriate value of $\underline{J}$ will then allow a corrected $\underline{I}$ to be calculated for each strong reflexion.

1.3 Structure Factors

Structure factors provide the link between the observed data and the calculated electron density distribution. They are defined by two quantities, an amplitude $|F|$ and a phase angle $\underline{\alpha}$. $|F|$ is directly related to the measured intensity, $\underline{I}$, by:

$$|F| \propto I^{\frac{1}{2}} \qquad (7)$$

It can be shown that for any reflexion, $\underline{hkl}$, the structure factor F(hkl) is given by:

$$F(hkl) = \sum_{j=1}^{N} f_j \exp 2\pi i (hx_j + ky_j + lz_j) \qquad (8)$$

Where atom $\underline{j}$ is situated at a point defined by the fractional atomic coordinates $(x_j\ y_j\ z_j)$ and has an atomic scattering factor $\underline{f}_j$.

Equation (8) may also be expressed in terms of its real and imaginary parts, $\underline{A}$ and $\underline{B}$, respectively, so that:

$$F = A + iB \qquad (9)$$

where $$A = \sum_{j=1}^{N} f_j \cos 2\pi (hx_j + ky_j + lz_j)$$

and $$B = \sum_{j=1}^{N} f_j \sin 2\pi (hx_j + ky_j + lz_j)$$

The amplitude and phase of F(hkl) are then given by:

$$|F(hkl)| = (A^2+B^2)^{\frac{1}{2}} \qquad (10)$$

and $\alpha(hkl) = \tan^{-1}(B/A)$

The term $\underline{f}_j$ in equation (8) and subsequent equations is a function of atom type and $\sin(\theta/\lambda)$ It is expressed in terms of the appropriate number of electrons located at the centre of the atom (e.g. C = 12). Its value diminishes with $\sin(\theta/\lambda)$ because the finite size of the electron cloud produces phase differences between waves scattered from distinct points within its volume.

Thermal motion causes the electron density to distribute itself over a larger volume with increasing temperature. The resulting reduction in atomic scattering power is greater for higher values of $\sin(\theta/\lambda)$

For isotropic vibration the scattering factor is given by:

$$f_j = f_o \exp\left[-B(\sin^2\theta)/\lambda^2\right] \qquad (11)$$

where f_o = the scattering power of stationary atom

$B = 8\pi^2\bar{U}^2$ the Debye-Waller factor

$\bar{U}^2$ = the mean square amplitude of the atomic displacement at right angles to the reflecting plane.

and for anisotropic vibration: (12)

$$f_j = f_o \exp\left[-(B_{11}h^2a^{*2} + B_{22}k^2b^{*2} + B_{33}l^2c^{*2} + 2B_{12}hka^{**}b^{**} + 2B_{13}hlac^{**} + 2B_{23}klbc^{**})/4\right]$$

Where B_{11}, B_{22} etc. are the anisotropic components of the term $\underline{B}$ in equation (11) and a^*, b^*, c^*, are the lengths of the reciprocal cell edges.

Debye-Waller factors are sometimes expressed in terms of $\underline{U}$ where $\underline{U} = \bar{U}^2 = B/8\pi^2 = B/78.96$

1.4 Structure factors and the electron density distribution

Any quantity such as the electron density $\rho(xyz)$ which varies periodically may be analysed into a number of separate basic components which when superimposed represent that quantity. This method of analysis is due to the French physicist J.B. Fourier and the three dimensional summation for electron density gives:

$$\rho(xyz) = \frac{1}{V} \sum_{-\infty}^{+\infty} \sum \sum F(hkl) \exp\left[-2\pi i(hx+ky+lz)\right] \qquad (13)$$

Thus if $F(hkl)$ is known then equation (13) will reproduce the electronic distribution in the crystal. Unfortunately, only $|F(hkl)|$ is immediately available from the intensity measurements and the phase angle $\underline{\alpha}$ must still be determined. For centrosymmetric space groups $\underline{\alpha}$ can only take on values of 0 or π but for non-centrosymmetric cells it may assume a whole range of magnitudes and it is more convenient to rewrite equation (13) as:

$$\rho(xyz) = \sum_{-\infty}^{+\infty} \sum_h \sum_k \sum_l \frac{|F(hkl)|}{V} \exp\left[2\pi i(hx+ky+lz) - \alpha(hkl)\right] \qquad (14)$$

Where $\alpha(hkl)$ is the phase angle appropriate to $|F(hkl)|$.

There are a number of methods for obtaining the elusive $\alpha(hkl)$ and the following section describes the general approach made to this problem by contemporary crystallography.

1.5 Direct Methods of phase determination

Modified structure factors

Direct methods rely on comparing the relative values of related intensities, but because scattering power is not independant of the Bragg angle, this comparison is less straightforward than might at first appear. High angle reflexions are considerably diminished by the fall-off in scattering ability and "reflexions" may be unobserved. A correction can be applied using a unitary structure factor $\underline{U}(h)$ instead of $\underline{F}(h)$ so that:

$$U(h) = F(h) \Big/ \sum_{J=1}^{N} f_J \qquad (15)$$

Where the summation is carried out over the $\underline{N}$ atoms in the molecule and $\underline{f_J}$ is the scattering factor for atom $\underline{J}$ compensating for both theta fall-off and thermal effects as discussed in 1.3

This equation (15) expresses each structure factor as a proportion of its maximum possible value for the particular magnitude of theta at which it occurs. Thus all unitary structure factors must lie within the range ± 1.

The extrema corresponding to those instances where all the atoms scatter in phase and hence restricting possible atomic sites. Values of ± 1 are rarely observed but greater constraints are placed on atomic location with increasingly closer approach to unity. However, the average value of $\underline{U}$ is dependent on the number of atoms, $\underline{N}$, in the molecule and for reasonably sized molecules there may be so few large $\underline{U}$s that an insufficient number of relationships can be established. Equation(16) gives the root mean square value of $\underline{U}$, $\underline{U}_{rms}$, in terms of the total scattering power represented by each atom:

$$U_{rms} = \sum_{1}^{N} (n_i^2)^{\frac{1}{2}} \qquad (16)$$

where $n_i = f_i / \Sigma_j f_j$

A normalised structure factor, $\underline{E}(h)$, may be obtained by relating each structure factor to $\underline{U}_{rms}$ and thus the difficulty arising with increasing $\underline{N}$ can be overcome. This gives:

$$E(h)^2 = |F(h)|^2 / \sum_{i=1}^{N} f_i^2 \qquad (17)$$

Under some circumstances space group symmetry produces special sets of reflexions which are abnormally higher (or lower) than the calculated average and the $\underline{E}$ values for these must be modified by a factor $\underline{\varepsilon}$ thus:

$$E(h)^2 = |F(h)|^2 / \varepsilon \sum_{i=1}^{N} f_i^2 \qquad (18)$$

The distribution of $|\underline{E}|$ gives an indication of the centricity or otherwise of the space group involved.

Inequality relationships

The unitary and normalised structure factors may be expressed in exactly the same way as ordinary structure factors:

$$U(h) = 2 \sum_{i}^{N/2} n_i \cos 2\pi h x_i \qquad (19)$$

for a centrosymmetric space group.

Harker and Kasper found that they were able to represent equation (19) in terms of a classical Cauchy inequality and obtained the relationship:

$$|U(h)|^2 \leqslant \tfrac{1}{2}\left[1 + U(2h)\right] \qquad (20)$$

This important equation allows the structure factor of an h (or hkl) reflexion to be compared with a 2h (or 2h 2k 2l) and may enable a phase determination to be made. Similar inequalities can be derived for other symmetry elements. Inequality relationships on their own are, however, of limited value, as the number of atoms increases, since definite determination requires large values of U.

Probability methods

Inequalities represent the limiting case of probability methods which in general produce phases which are less reliable. Much of the early work to combine probability theory with inequalities is due to (a) Sayre and (b) Cochrane and Woolfson.

The basic relationships are:

$$\text{(a)} \quad S(F_{hkl}) \backsimeq S(F_{h'k'l'}) \,.\, S(F_{h-h'\ k-k'\ l-l'}) \qquad (21)$$

$$\text{(b)} \quad P(E) = \tfrac{1}{2} + \tfrac{1}{2}\tanh\left(\left|E_{hkl} E_{h'k'l'} E_{h-h'\ k-k'\ l-l'}\right| . N^{-\frac{1}{2}}\right)$$

In equation (21a) $\underline{S}(F_{hkl})$ means the sign of the structure amplitude $|F_{hkl}|$. $\underline{S}(F_{hkl})$ may be replaced by $\underline{\theta}(F_{hkl})$, thus allowing the Sayre expression to be used for non-centrosymmetric space groups. The starting magnitudes and/or signs must obviously be reliable in order to yield reasonable atomic co-ordinates.

Equation 21b) expresses in terms of $\underline{E}$ values the probability, $\underline{P(E)}$, that for a given $\underline{hkl}$ and related pair of reflexions, the relationship in equation(21a) is true.

Practical phase determination

The best known application of equations (21) is probably the symbolic addition method of the Karles which is the basis of the program MULTAN (Main and Woolfson).

The principal subprograms are:

(a) The SIGMA 2 program which derives $|\underline{E}|$ from the observed data and then uses the largest values to set up all the triple relationships of the form expressed by equation (33a).

(b) CONVERGE uses the supplied space group information to decide which parity groups are required to define the origin and then calculates the probabilities for the signs of the structure invariants. By a process of elimination the program should eventually be able to converge on the best starting set.

(c) FASTAN uses this starting set to determine the phases of other high value $|\underline{E}|$s. As the non-origin

defining reflexions in the starting set may take on more than one value several complete sets of phases may be generated from the Σ2 phase relationships. Each reflexion with $|\underline{E}|$ above a specified value will have its phase calculated and this phase may be assigned a weight which is related to the probability of it being correct. FASTAN, by using a weighted version of the tangent formula puts less emphasis on the poorly determined phases in subsequent phase development and thus allows rapid convergence on the most consistent complete set from each starting combination. A figure of merit based on the degree of internal consistency is given to each complete phase set.

(d) FOURIER computes an $\underline{E}$ map using the set showing the best figure of merit from which it should be possible to recognise atomic sites.

MULTAN does not always give a correct solution. This may be due to a number of reasons, for example, poorly diffracting crystals, unreliable data, a large number of atoms in the asymmetric unit, or the particular space group concerned.

1.6 Fourier Synthesis

Phases obtained by direct or other methods are only approximate and must be further refined to yield a more accurate structure. This is achieved by combining the calculated phases with the observed amplitudes in a summation such as that represented by equation (14).

The resulting electron density distribution will not be very accurate, but it should give a better indication of atomic sites. These new atom locations can then be used in a second Fourier synthesis to work backwards and yield a calculated set of structure factors (Fc) and more accurate phases. The process may be continued in this manner until the atomic parameters cease to change significantly.

A further Fourier summation can then be carried out based on the quantity (Fo-Fc). This will reveal any non-hydrogen atoms inadvertently missed during the Fo synthesis and often indicates the position of many of the hydrogen atoms.

1.7 Least squares refinement

Fourier summation as described above will contain termination of series errors, since the amount of data is finite. The reasonably correct atomic locations available from the Fourier synthesis may now be further refined by the method of least squares. This method is based on the principle that the best fit, between observed data and related functional equations, is obtained when the sum of the squares of the differences between observed and calculated values is a minimum. The function, D, is the one most commonly used:

$$D = \sum_{hkl} W(|Fo| - |Fc|)^2 = \sum_{hkl} W\Delta^2 \qquad (22)$$

Where W is a measure of the accuracy of each observation.

If the variables affecting $|Fc|$ are represented by $\underline{P_1}, \underline{P_2}, \ldots \underline{P_j} \ldots \underline{P_n}$ then the stationary value of equation (22) is given by:

$$\frac{\delta D}{\delta P_j} = 0 = \sum_{hkl} W \Delta \frac{\delta |Fc|}{\delta P_j} \quad (j = 1,n) \qquad (23)$$

These $\underline{n}$ equations (23) have a solution which will give the best values of the parameters $\underline{P_j}$. The large number of equations involved for an average sized structure cannot be solved easily. However, values for the $\underline{P_j}$ are already available from the $\underline{Fo}$ summation and at this stage only small changes, $\underline{\varepsilon}$, should be required. The total change $\underline{\Delta}$ may be expanded as a truncated Taylor series:

$$\Delta(P+\varepsilon) = \Delta P - \sum_{i=1}^{n} \varepsilon_i \frac{\delta |F_c|}{\delta P_i} \qquad (24)$$

Where subscripted/non-subscripted variables refer to individual/total changes and parameters.

Combination of equations (23) and (24) gives a set of normal equations:

$$\sum_{i=1}^{n} \left\{ \sum_{hkl} w \frac{\delta |F_c|}{\delta P_i} \cdot \frac{\delta |F_c|}{\delta P_j} \right\} \varepsilon_i = \sum_{hkl} w \Delta \frac{\delta |F_c|}{\delta P_j}$$

The normal equations may be written as:

$$\sum_i a_{ij} \varepsilon_i = b_j \quad (j = 1,2 \ldots . n) \qquad (25)$$

Solution of these sets of normal equations will yield the shifts $\underline{\varepsilon_i}$ and the calculation may be repeated to convergence by using the new $\underline{P_j}$ from one cycle as the starting point for the following one.

Least squares refinement can be carried out using either block diagonal or full matrix techniques. The saving in computer time and storage for the former must be offset against the possibility that the off-diagonal relationships are not small.

The errors in the final set of atomic co-ordinates may be estimated from the following expression:

$$\sigma(P_i) = \left[(a^{-1})_{ii} \frac{\Sigma W \Delta^2}{m - n} \right]^{\frac{1}{2}} \qquad (26)$$

Where $\sigma(P_i)$ is the error in parameter P_i.

$(a^{-1})_{ii}$ is the inverse of a matrix of the form represented by equation (25).

m is the number of observations.

n is the number of parameters.

The quantity $\underline{W}$ should be given by:

$$W(hkl) = \frac{1}{\sigma^2(hkl)}$$

Where $\sigma^2(hkl)$ is the esd of the amplitude $|Fo(hkl)|$ and this could be determined by repeated observations of each reflexion. This is clearly impracticable for a large body of data and an empirical weighting scheme is usually employed instead. Such schemes are designed to keep the function $W(|Fo| - |Fc|)^2$ constant when averaged over batches of data.

The quality of fit obtained in a least squares refinement may be expressed in terms of a weighted residual, $\underline{R}$:

$$R = \frac{\Sigma w(|Fo| - |Fc|)^2}{\Sigma w |Fo|^2} \qquad (27)$$

CHAPTER TWO

X-ray diffraction studies of the sesquiterpenoids costunolide and mikanokryptin

2.1 Foreword

Sesquiterpenoids are C15 compounds which may be considered (1,2) to be built up from three isoprenoid units. A number of different cyclisations of the C15 precursor can occur giving rise to the wide diversity of structural types currently known. The most common carbon skeletons (3) are illustrated in Fig. 2.1.

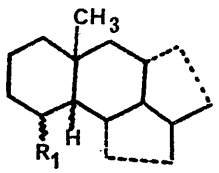
The germacranolides are particularly important because they are believed to be intermediates in the biogenesis of some other sesquiterpenes (e.g. guianolides). The x-ray analyses of the two sesquiterpenes in this chapter have been carried out to provide conformational information both to assist in biogenetic investigations and as part of a study of medium ring dienes.

2.2 Costunolide

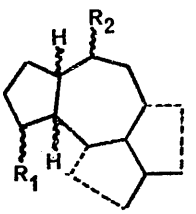
Costunolide (I), a germacranolide, has been extracted from the plant, Saussurea lappa Clarke (4), found in the Himalayas and from Artemisia balchanorum H. Krasch (5), which occurs in Central Asia. Professor Kupchan, (University of Virginia) kindly supplied the sample of costunolide used in the analysis which follows.

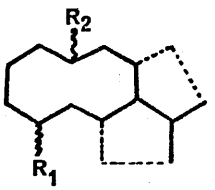
Previous work by diffraction (5, 6), synthetic (7) and IR (8) methods on costunolide and its silver nitrate adduct failed to yield the complete structure. The evidence from these studies for the proposed conformation (Fig. 2.2) was supported by the work of Tori et al (9)

Anolide

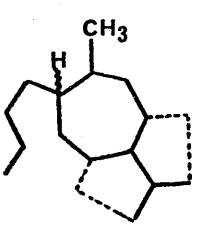


Guianolide

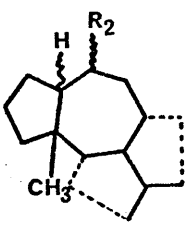




Germacranolide



Xantholide

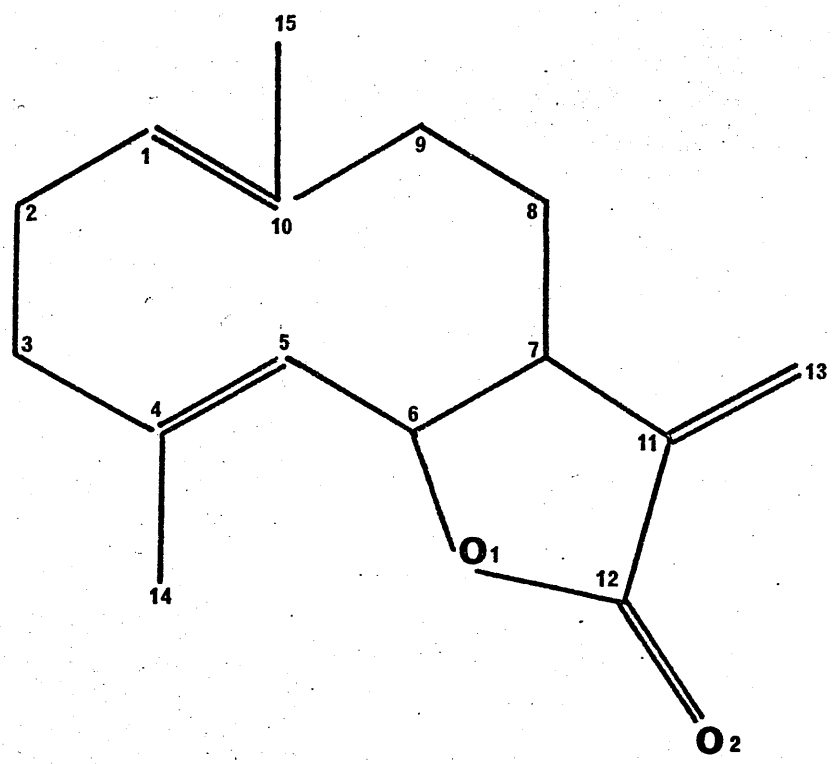


Ambrosanolide

R_1 = CH_3 or H

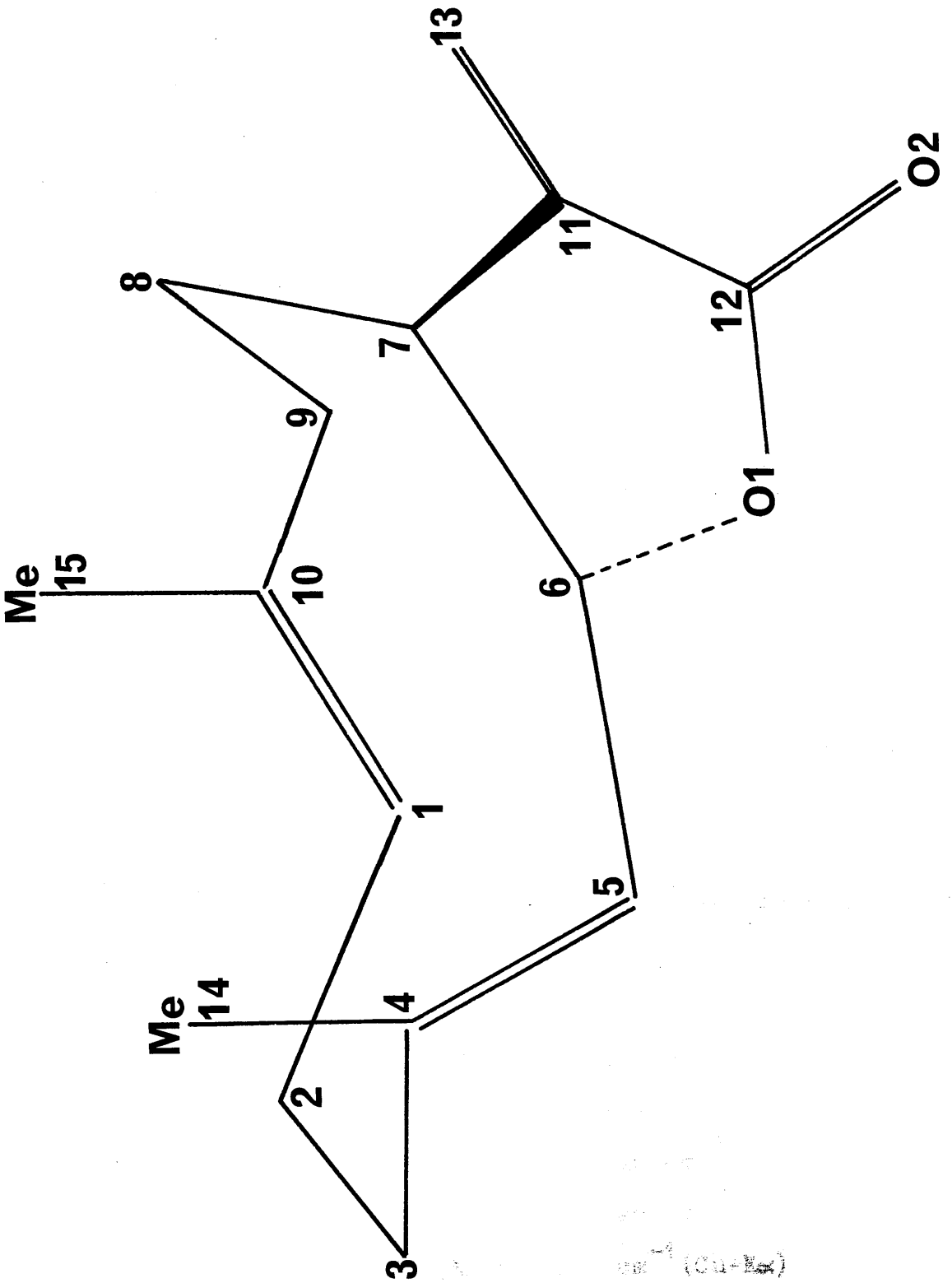
R_2 = CH_3 or H

Fig.2.1 Sesquiterpenoids: Most frequently occurring skeletons



(I)

Fig. 2.2 Structure of Costunolide


13
O2
11
8
12
7
9
O1
Me
15
10
6
1
5
Me
14
4
2
3

based on the simultaneous application of the nuclear overhauser effect and an NMR shift reagent, and by the ORD/CD results of Suchy and co-workers (10).

The earlier x-ray analyses (5,6) had used Mo-Kα radiation for four circle diffractometer measurement of intensities for costunolide (6) and its silver nitrate adduct (5) but had not revealed the hydrogen atoms. Further, the effect of the silver nitrate on the conformation of the macrocycle was not clear. It was decided to recollect intensity data using Cu-Kα radiation in the hope that some of the weaker reflexions could be included and thus provide a more accurate structure.

2.3 Experimental

Crystal data

Costunolide $C_{15}H_{20}O_2$

Unit cell dimensions $\underline{a} = 11.028$ A^{o}

$\underline{b} = 15.400$ A^{o} $\alpha = \beta = \gamma = 90^{o}$

$\underline{c} = 7.987$ A^{o}

Space group $P2_12_12_1 (D_2^4)$

M = 232 a.m.u.

V = 1356 A^{o3}

Do= 1.159 gm cm^{-3}

Dc= 1.136 gm cm^{-3}

μ = 5.9 cm^{-1} (Cu-Kα)

F(000) = 504

Z = 4

The space group was determined uniquely by the systematic absences:

h00 when h=2n+1, 0k0 when k=2n+1, 00l when l=2n+1.

The crystal used in this analysis was a small cube with a 1mm side.

Data Collection

Cell measurements were available from the previous analysis and these were confirmed from precession photographs. The crystal was transferred to a Hilger & Watts Y290 four circle diffractometer controlled by a PDP-8 computer. Cu-Kα radiation filtered through nickel was employed.

The positions of the reciprocal axes with respect to the crystal faces were approximately known from the photographic work and a starting pair of reflexions was obtained by scanning the $\underline{\Phi}$ circle at $\underline{2\theta}$ values calculated from the cell dimensions. These reflexions were optimised by $\underline{2\theta}$, $\underline{\Phi}$ and $\underline{\chi}$ scans and indexed to obtain an initial orientation matrix. This orientation matrix was then used to calculate the angular settings for a further 15 reflexions which were also optimised as described above. The unit cell parameters were refined using these 17 setting angles in a least squares procedure and are quoted in the crystal data.

Intensity measurements were made with the $\underline{\theta, 2\theta}$ scan procedure. Typical scan parameters were as follows:

Increment in $\underline{\theta}$ = 0.01°

No. of scan steps = 80

Time per step = 1 sec.

Background counts were made for 20 seconds at each extreme position of the scan.

The integrated intensity, $\underline{I}$, was calculated from the peak, $\underline{P}$, and background $\underline{B1}$, $\underline{B2}$, counts using equation (1):

$$I = P-(B1+B2).\frac{tp}{2tb} \qquad (1)$$

tp = counting time at peak.

tb = " " for one of the background counts (both the same).

and the standard deviation of $\underline{I}$, (σI), was obtained from equation (2):

$$\sigma I = \left(P+(B1+B2)\frac{tp}{2tb}\right)^{\frac{1}{2}} \qquad (2)$$

Two strong reflexions were used as standards throughout the data collection. Their counts were checked after every 20 intensity measurements. These monitor counts held constant to within about 2 % during the data collection and were used to place all the measurements on a common scale.

Reflexion intensities were collected for $2\theta \leq 110^{\circ}$ in the two equivalent octants $\underline{hkl}$, $\underline{h\bar{k}\bar{l}}$. Data for which $I \leq 2\sigma I$ were discarded and equivalent reflexions were averaged to give 1398 independant structure amplitudes.

A number of reflexions had high counts which may have saturated the counter. Accordingly data for which $2\theta \leq 20^{\circ}$ were recollected with a reduced beam intensity so that a counting loss correction could be applied.

Structure Analysis

A trial set of non-hydrogen co-ordinates was available from the Mo-Kα analysis and these gave an initial residual R of 25.2% with fixed isotropic temperature factors. Four cycles of least squares refinement of these co-ordinates, allowing for anisotropic thermal motion, reduced R to 14.4%. A difference synthesis was carried out and this yielded most of the hydrogen atoms. These hydrogen locations were refined with invariant isotropic temperature factors during a further two cycles of least squares calculations. A new difference synthesis yielded the remaining hydrogen atoms. Two further cycles of full matrix least squares adjustment, during which the isotropic thermal parameters of the hydrogen atoms were also refined, converged at R = 7.9%

Counting loss errors were then corrected and this gave an R of 6.8%. Finally a weighting scheme of the form:

$W = x.y$ Where the weight, W, was calculated as follows,

(a) For $0.7|Fo| > |Fc|$, $W = 1 \times 10^{-9}$ otherwise,

(b) $x = \sin\theta/2.1$

(c) $y = 1$, unless $|Fo| > 3.05$ when $y = 3.05/|Fo|$

(x and y were selected to minimize the deviation from constant $W\Delta^2$ over the whole range of $\sin\theta$ and $|Fo|$).

was applied and after two cycles of least squares calculations a value of R=4.3% resulted. The ratio of observations to parameters was 6.0 to 1 and no correction was made for absorption.

2.4 Results

Table I Costunolide: Fractional atomic coordinates

Positional estimated standard deviations are shown in parentheses.

The hydrogen atoms are numbered according to the atoms to which they are attached.

The table shows:

Atom	x	y	z

C(1)	0876(2)	6935(1)	1874(3)
C(2)	-0116(2)	6850(2)	3117(4)
C(3)	0073(2)	6014(2)	4177(4)
C(4)	1345(2)	6021(1)	4881(3)
C(5)	2222(2)	5671(1)	3959(2)
C(6)	3533(2)	5880(1)	4067(2)
C(7)	4125(2)	6064(1)	2351(2)
C(8)	4083(2)	7009(1)	1742(3)
C(9)	2919(2)	7313(1)	0836(3)
C(10)	1841(2)	7448(1)	1951(2)
C(11)	5381(2)	5709(1)	2628(3)
C(12)	5322(2)	5093(1)	4052(4)
C(13)	6414(3)	5851(2)	1855(5)
C(14)	1566(3)	6526(2)	6435(3)
C(15)	1967(3)	8182(2)	3166(4)
O(1)	4218(1)	5144(1)	4768(2)
O(2)	6080(2)	4591(1)	4551(4)
H(1)	0951(22)	6544(16)	1014(32)
H(21)	-0049(26)	7476(19)	3876(37)
H(22)	-0944(29)	6786(22)	2608(45)
H(31)	-0574(32)	5978(23)	5088(55)
H(32)	-0114(39)	5484(27)	3342(58)
H(5)	1972(21)	5289(14)	2937(30)
H(6)	3712(20)	6360(15)	4868(32)
H(7)	3717(26)	5699(20)	1526(39)
H(81)	4256(30)	7465(23)	2759(44)
H(82)	4772(29)	7079(21)	1043(41)
H(91)	3098(24)	7905(17)	0222(35)
H(92)	2775(22)	6848(16)	-0001(33)
H(131)	7251(39)	5485(27)	2284(59)
H(132)	6429(19)	6113(14)	1318(29)
H(141)	2401(29)	6544(20)	6770(42)
H(142)	1045(30)	6359(23)	7281(44)
H(143)	1362(32)	7123(25)	6224(51)
H(151)	1236(43)	8261(32)	3903(64)
H(152)	2435(38)	8662(30)	2776(58)
H(153)	2492(53)	8000(38)	4211(73)

Table II Costunolide: Thermal parameters

Carbon and oxygen values are anisotropic.
Hydrogen values are isotropic.

Estimated errors in the last two digits are shown in parentheses.

All figures are multiplied by 10^4.

The anisotropic temperature factor expression used was of the form described by equation (12) in chapter one, the coefficients being in terms of the mean square amplitudes of vibration U_{ij} .

The table shows:

Atom	U_{11} or U	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}

C(1)	824(12)	800(11)	734(11)	21(10)	-172(10)	60(10)
C(2)	693(11)	1059(16)	1112(18)	81(11)	-80(13)	204(15)
C(3)	676(11)	1014(16)	1148(18)	51(11)	147(12)	253(15)
C(4)	735(10)	770(10)	751(11)	77(9)	141(9)	201(10)
C(5)	683(9)	615(9)	698(10)	-6(8)	94(9)	64(8)
C(6)	684(9)	579(8)	618(9)	29(7)	26(8)	34(7)
C(7)	697(9)	645(9)	618(9)	-85(8)	39(8)	0(8)
C(8)	798(12)	796(12)	883(14)	-144(10)	23(11)	213(12)
C(9)	1011(14)	878(13)	694(11)	-42(12)	7(12)	248(10)
C(10)	898(12)	676(9)	645(9)	-14(10)	-123(9)	107(9)
C(11)	704(10)	695(10)	883(13)	-41(8)	120(10)	-97(10)
C(12)	698(10)	763(11)	1095(16)	64(10)	-6(12)	20(12)
C(13)	894(16)	1169(20)	1444(25)	-88(15)	358(18)	110(21)
C(14)	1059(17)	1209(19)	702(13)	289(16)	208(12)	45(13)
C(15)	1381(23)	818(14)	1061(18)	-198(15)	48(19)	-117(14)
O(1)	773(7)	809(8)	889(9)	137(6)	66(7)	236(8)
O(2)	875(10)	1078(12)	1754(22)	289(10)	-13(13)	301(15)
H(1)	590(61)					
H(21)	822(81)					
H(22)	897(96)					
H(31)	884(114)					
H(32)	1074(143)					
H(5)	458(57)					
H(6)	440(57)					
H(7)	584(79)					
H(81)	937(98)					
H(82)	827(87)					
H(91)	694(68)					
H(92)	624(64)					
H(131)	1287(146)					
H(132)	563(53)					
H(141)	781(89)					
H(142)	859(100)					
H(143)	935(112)					
H(151)	1267(159)					
H(152)	1238(132)					
H(153)	1670(210)					

TABLE III

COSTUNOLIDE: INTRAMOLECULAR BONDED DISTANCES(ANGSTROMS)
STANDARD DEVIATIONS (ANGSTROMS) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	DIST.	ATOM1	ATOM2	DIST.
C1	C2	1.484(3)	C2	H21	1.123(27)
C1	C10	1.326(2)	C2	H22	1.008(32)
C2	C3	1.555(3)	C3	H31	1.033(39)
C3	C4	1.512(3)	C3	H32	1.052(37)
C4	C5	1.329(2)	C5	H5	1.046(24)
C4	C14	1.486(3)	C6	H6	0.988(21)
C5	C6	1.483(2)	C7	H7	0.972(27)
C6	C7	1.544(3)	C8	H81	1.081(38)
C6	O1	1.473(1)	C8	H82	0.942(33)
C7	C8	1.536(2)	C9	H91	1.056(23)
C7	C11	1.506(2)	C9	H92	0.997(26)
C8	C9	1.546(3)	C13	H131	1.113(38)
C9	C10	1.500(3)	C13	H132	0.665(27)
C10	C15	1.497(3)	C14	H141	0.976(28)
C11	C12	1.482(3)	C14	H142	0.931(36)
C11	C13	1.313(3)	C14	H143	0.952(25)
C12	O1	1.348(2)	C15	H151	1.006(47)
C12	O2	1.205(2)	C15	H152	0.989(37)
C1	H1	0.978(29)	C15	H153	1.035(64)

TABLE IV COSIUNOLIDE: INTERMOLECULAR CONTACTS OF LESS THAN 4.0 ANGSTROMS

ATOM1	ATOM2		DIST #	ATOM1	ATOM2		DIST #
C(3)	C(4)	*	3.859	O(2)	C(2)	*	3.764
C(3)	C(13)	*	3.938	O(2)	C(13)	**	3.389
C(4)	C(7)	*	3.803	C(8)	C(14)	***	3.835
C(4)	C(11)	*	3.941	C(12)	C(15)	***	3.910
C(14)	C(12)	*	3.864	C(9)	O(2)	****	3.691
C(14)	O(1)	*	3.802	C(15)	O(2)	****	3.748
O(1)	C(1)	*	3.618	C(8)	C(1)	*****	3.860
O(1)	C(5)	*	3.912	C(13)	C(9)	*****	3.921
O(2)	C(1)	*	3.691				

IN ANGSTROMS

THE ASTERISKS(*) REFER TO THE FOLLOWING TRANSFORMATIONS OF THE ATOMIC COORDINATES

*	0.5-X, 1.0-Y, 0.5+Z
**	1.5-X, 1.0-Y, 0.5+Z
***	0.5+X, 1.5-Y, 1.0-Z
****	1.0-X, 0.5+Y, 0.5-Z
*****	0.5+X, 1.5-Y, -Z

TABLE V

COSTUNOLIDE: VALENCY ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ANGLE	ATOM1	ATOM2	ATOM3	ANGLE
C10	C1	C2	127.7(2)	C3	C2	C1	109.7(1)
C4	C3	C2	108.8(1)	C5	C4	C3	117.8(2)
C14	C4	C3	117.8(2)	C14	C4	C5	123.8(1)
C6	C5	C4	126.1(1)	C7	C6	C5	113.7(1)
O1	C6	C5	110.8(1)	O1	C6	C7	105.2(1)
C8	C7	C6	116.2(1)	C11	C7	C6	101.1(1)
C11	C7	C8	114.8(1)	C9	C8	C7	117.4(1)
C10	C9	C8	115.0(2)	C15	C10	C1	123.8(2)
C9	C10	C1	121.7(1)	C15	C10	C9	114.5(1)
C12	C11	C7	107.8(1)	C13	C11	C7	131.8(2)
C13	C11	C12	120.4(2)	O1	C12	C11	109.1(1)
O2	C12	C11	129.2(2)	O2	C12	O1	121.7(2)
C12	O1	C6	110.4(1)	H1	C1	C2	119.9(14)
H1	C1	C10	111.5(14)	H22	C2	C1	114.7(24)
H21	C2	C1	103.2(16)	H21	C2	C3	113.7(18)
H22	C2	C3	106.0(16)	H22	C2	H21	109.8(21)
H32	C3	C2	104.4(21)	H31	C3	C4	112.6(22)
H32	C3	C4	113.8(18)	H31	C3	C2	108.8(14)
H32	C3	H31	108.1(26)	H5	C5	C4	118.1(11)
H5	C5	C6	114.9(11)	H6	C6	O1	103.4(12)
H6	C6	C5	112.5(11)	H6	C6	C7	110.6(13)
H7	C7	C11	108.5(12)	H7	C7	C6	106.7(16)
H7	C7	C8	109.0(14)	H81	C8	C9	108.4(16)
H82	C8	C9	110.6(21)	H82	C8	C7	105.1(13)
H81	C8	C7	110.5(18)	H82	C8	H81	103.9(26)

VALENCE_ANGLES (CONTINUED)

ATOM1	ATOM2	ATOM3	ANGLE	ATOM1	ATOM2	ATOM3	ANGLE
H92	C9	C10	112.1(14)	H91	C9	C8	109.0(14)
H92	C9	C8	103.0(13)	H91	C9	C10	107.0(15)
H92	C9	H91	110.7(24)	H131	C13	C11	119.3(25)
H132	C13	C11	119.9(19)	H132	C13	H131	120.8(31)
H142	C14	C4	111.5(20)	H143	C14	C4	107.3(28)
H141	C14	C4	113.2(20)	H142	C14	H141	113.0(31)
H143	C14	H141	104.7(22)	H143	C14	H142	106.5(28)
H152	C15	C10	114.7(30)	H153	C15	C10	112.7(24)
H151	C15	C10	111.6(23)	H152	C15	H151	124.0(28)
H153	C15	H151	91.0(44)	H153	C15	H152	98.5(39)

TABLE VI

COSTUNOLIDE: TORSION ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
C10	C1	C2	C3	-101.9(2)	C2	C1	C10	C9	164.7(2)
C2	C1	C10	C15	-13.5(3)	C1	C2	C3	C4	52.2(2)
C2	C3	C4	C5	-88.7(2)	C2	C3	C4	C14	82.8(2)
C3	C4	C5	C6	155.9(1)	C14	C4	C5	C6	-15.0(3)
C4	C5	C6	C7	-131.2(1)	C4	C5	C6	O1	110.6(2)
C5	C6	C7	C8	88.7(1)	C5	C6	C7	C11	-146.4(1)
O1	C6	C7	C8	-149.9(1)	O1	C6	C7	C11	-25.0(1)
C5	C6	O1	C12	145.1(1)	C7	C6	O1	C12	21.9(1)
C6	C7	C8	C9	-84.0(2)	C11	C7	C8	C9	158.4(1)
C6	C7	C11	C12	20.5(1)	C6	C7	C11	C13	-159.8(2)
C8	C7	C11	C12	146.4(1)	C8	C7	C11	C13	-33.9(3)
C7	C8	C9	C10	73.6(2)	C8	C9	C10	C1	-111.7(2)
C8	C9	C10	C15	66.6(2)	C7	C11	C12	O1	-8.5(2)
C7	C11	C12	O2	170.0(2)	C13	C11	C12	O1	171.8(2)
C13	C11	C12	O2	-9.7(4)	C11	C12	O1	C6	-8.7(2)
O2	C12	O1	C6	172.7(2)	C10	C1	C2	H21	19.6(15)
C10	C1	C2	H22	139.0(20)	H1	C1	C2	C3	66.4(17)
H1	C1	C2	H21	-172.1(23)	H1	C1	C2	H22	-52.7(27)
H1	C1	C10	C9	-4.4(16)	H1	C1	C10	C15	177.4(16)
C1	C2	C3	H31	175.2(19)	C1	C2	C3	H32	-69.6(20)
H21	C2	C3	C4	-62.8(16)	H21	C2	C3	H31	60.2(25)
H21	C2	C3	H32	175.4(26)	H22	C2	C3	C4	176.5(19)
H22	C2	C3	H31	-60.5(27)	H22	C2	C3	H32	54.7(28)
H31	C3	C4	C5	150.6(19)	H31	C3	C4	C14	-37.9(19)
H32	C3	C4	C5	27.1(21)	H32	C3	C4	C14	-161.3(21)

TORSION ANGLES (CONTINUED)

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
C3	C4	C5	H5	-12.4(13)	C14	C4	C5	H5	176.6(13)
C3	C4	C14	H141	-176.0(18)	C3	C4	C14	H142	55.3(20)
C3	C4	C14	H143	-61.0(21)	C5	C4	C14	H141	-5.0(19)
C5	C4	C14	H142	-133.7(20)	C5	C4	C14	H143	110.0(21)
C4	C5	C6	H6	-4.6(13)	H5	C5	C6	C7	37.4(12)
H5	C5	C6	O1	-80.8(12)	H5	C5	C6	H6	164.1(18)
C5	C6	C7	H7	-33.1(15)	O1	C6	C7	H7	88.3(15)
H6	C6	C7	C8	-39.0(12)	H6	C6	C7	C11	86.0(12)
H6	C6	C7	H7	-160.7(19)	H6	C6	O1	C12	-94.2(12)
C6	C7	C8	H81	41.0(19)	C6	C7	C8	H82	152.6(19)
C11	C7	C8	H81	-76.6(19)	C11	C7	C8	H82	35.0(19)
H7	C7	C8	C9	36.5(15)	H7	C7	C8	H81	161.5(24)
H7	C7	C8	H82	-86.9(24)	H7	C7	C11	C12	-91.4(15)
H7	C7	C11	C13	88.2(15)	C7	C8	C9	H91	-166.4(15)
C7	C8	C9	H92	-48.7(14)	H81	C8	C9	C10	-52.5(19)
H81	C8	C9	H91	67.5(24)	H81	C8	C9	H92	-174.8(24)
H82	C8	C9	C10	-165.8(19)	H82	C8	C9	H91	-45.8(25)
H82	C8	C9	H92	71.9(24)	H91	C9	C10	C1	127.2(15)
H91	C9	C10	C15	-54.5(15)	H92	C9	C10	C1	5.6(15)
H92	C9	C10	C15	-176.1(15)	C1	C10	C15	H151	-3.0(26)
C1	C10	C15	H152	-150.7(27)	C1	C10	C15	H153	97.7(32)
C9	C10	C15	H151	178.7(26)	C9	C10	C15	H152	31.1(27)
C9	C10	C15	H153	-80.5(32)	C7	C11	C13	H131	-177.6(24)
C7	C11	C13	H132	3.2(24)	C12	C11	C13	H131	2.1(25)

THE ANGLE 1-2-3-4 IS DEFINED AS POSITIVE IF, WHEN VIEWED ALONG THE 2-3 BOND, ATOM 1 HAS TO BE ROTATED CLOCKWISE TO ECLIPSE ATOM 4

TABLE VII COSTUNOLIDE: MEAN PLANE CALCULATIONS

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
1.	C(1)		0.000(2)
	C(2)		0.000(3)
	C(10)		0.000(2)
		C(15)	-0.291(3)
		H(1)	0.156(25)
2.	C(1)		0.000(2)
	C(9)		0.000(2)
	C(10)		0.000(2)
		C(15)	0.043(3)
		H(1)	-0.076(25)
3.	C(3)		0.000(3)
	C(4)		0.000(2)
	C(5)		0.000(2)
		C(14)	-0.197(3)
		H(5)	0.215(23)
4.	C(4)		0.000(2)
	C(5)		0.000(2)
	C(6)		0.000(2)
		C(14)	0.317(3)
		H(5)	-0.168(23)

TABLE VII (CONTINUED)

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
5.	C(11)		0.000(2)
	C(12)		0.000(3)
	O(1)		0.000(2)
		C(6)	0.212(2)
		C(7)	-0.209(2)
		C(13)	0.158(4)
		O(2)	-0.028(2)
6.	C(7)		0.000(2)
	C(11)		0.000(2)
	C(12)		0.000(3)
		C(6)	0.531(2)
		C(13)	-0.008(4)
		O(1)	0.186(2)
		O(2)	-0.164(2)
7.	C(13)		0.000(4)
	H(131)		0.000(44)
	H(132)		0.000(22)
		C(11)	0.055(2)

TABLE VII (CONTINUED)

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
8.	C(11)		-0.003(2)
	C(12)		0.008(3)
	O(1)		-0.003(2)
	O(2)		-0.003(2)
		C(6)	0.191(2)
		C(7)	-0.231(2)
		C(13)	0.163(4)

THE OUT OF PLANE ATOMS WERE NOT INCLUDED IN THE DERIVATION OF THE PLANES.

THE EQUATIONS OF THESE PLANES ARE:

1. $0.0510X - 0.7222Y + 0.4672Z = -6.5200$
2. $0.4081X - 0.6021Y + 0.6863Z = -5.0081$
3. $-0.1662X - 0.8870Y + 0.4308Z = -6.7909$
4. $0.1196X - 0.7199Y + 0.6837Z = -3.8317$
5. $0.3347X + 0.7143Y + 0.6146Z = 9.5561$
6. $0.1939X + 0.7481Y + 0.6347Z = 9.0594$
7. $0.1829X + 0.7115Y + 0.6784Z = 8.7100$
8. $0.3448X + 0.7064Y + 0.6182Z = 9.5564$

2.5 Discussion of Results

The results of the analysis are shown in Tables I - VII. Figs. 2.3 and 2.4 illustrate a view of the molecule, and of the crystal packing viewed along the c axis, respectively. The final and observed structure factors are listed in Table XIIa.

The extended chair conformation of the cyclodecadiene ring is very similar to that in a number of related sesquiterpenes (Fig. 2.5) as indicated in Table VIII. Strain energy calculations (15) have shown this to be the minimum energy conformation of trans, trans - cyclodeca-1,5-diene. The methyl substituents C(14) and C(15) are cis and β. This arrangement has also been observed in other germacranes e.g. eupatolide (11), alatolide (12), eupatoriopicrin (13), onopordopicrine (14), pregeijerene (16), germacratriene (17) and elephantol (18). Cis and α-(19) and anti- (20) stereochemistries are also known.

The C- C(sp^3) - C valency angles in the decadiene ring vary from 109° to 117° with a mean of 113.5°. These large deviations from the tetrahedral angle are indicative of considerable strain. This situation is quite common in saturated medium ring compounds many of which exhibit valency angles of 116 - 117° (21), and angles in excess of the tetrahedral value are not unusual (Table IX).

There is distortion of the double bonds at C(1) - C(10) and C(4) - C(5) as the respective torsion angles of 164° and 156° exhibit a marked departure from planarity Newman projections down these two bonds are shown in Fig. 2.6 and Table X describes the deformations in costunolide and some related structures in terms of τ (torsion) - and

Fig. 2.3 Costunolide: A view of the molecule

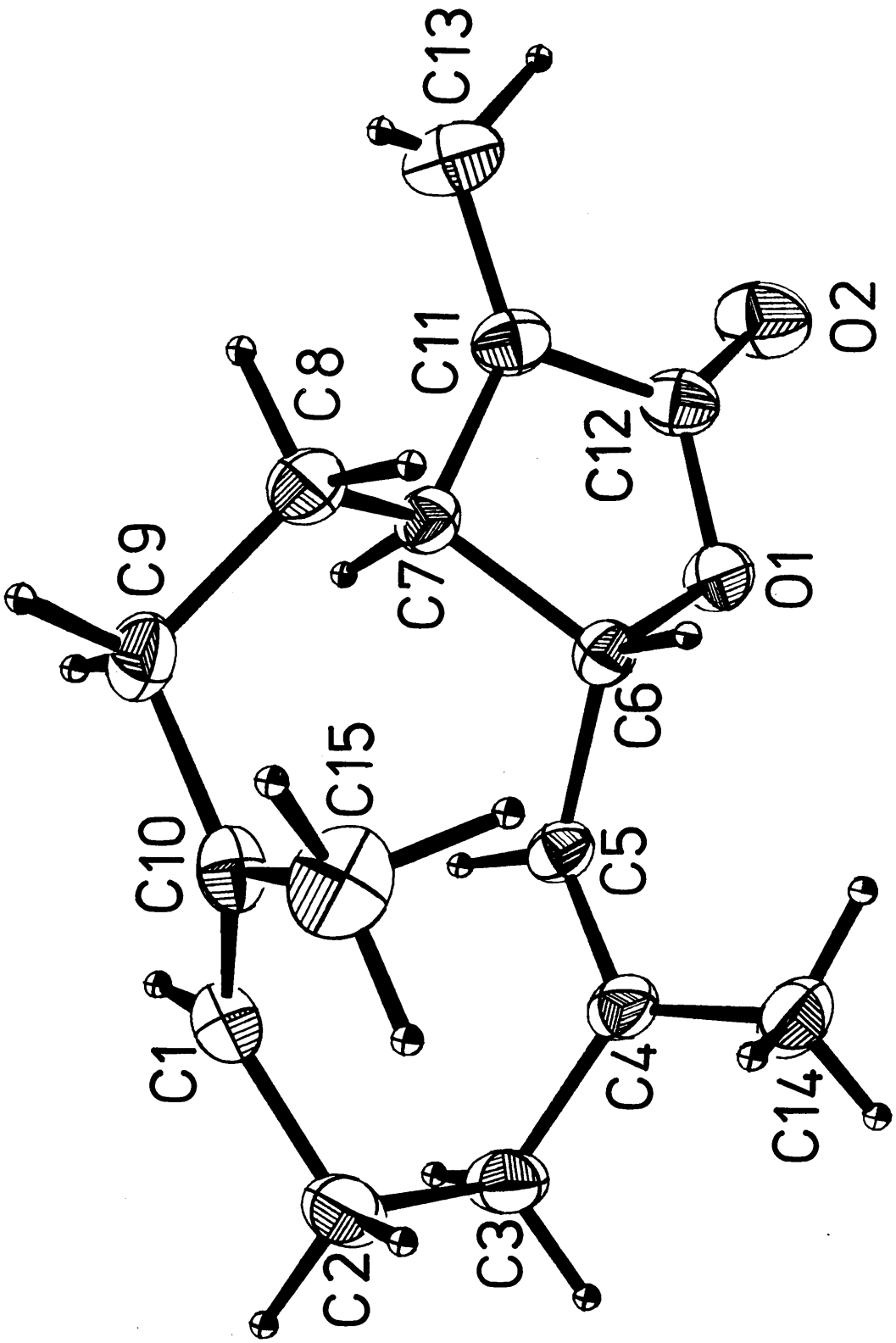
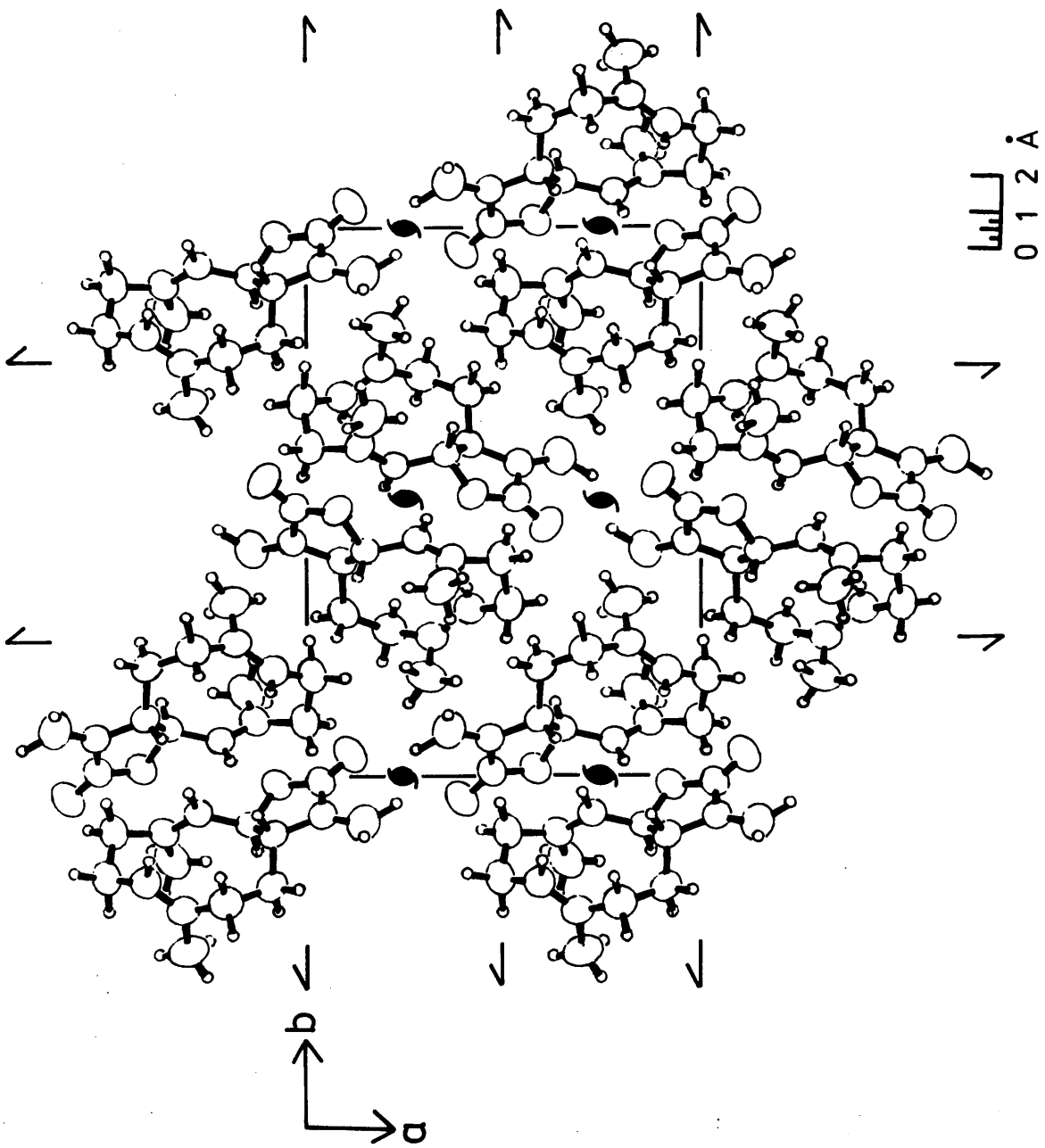
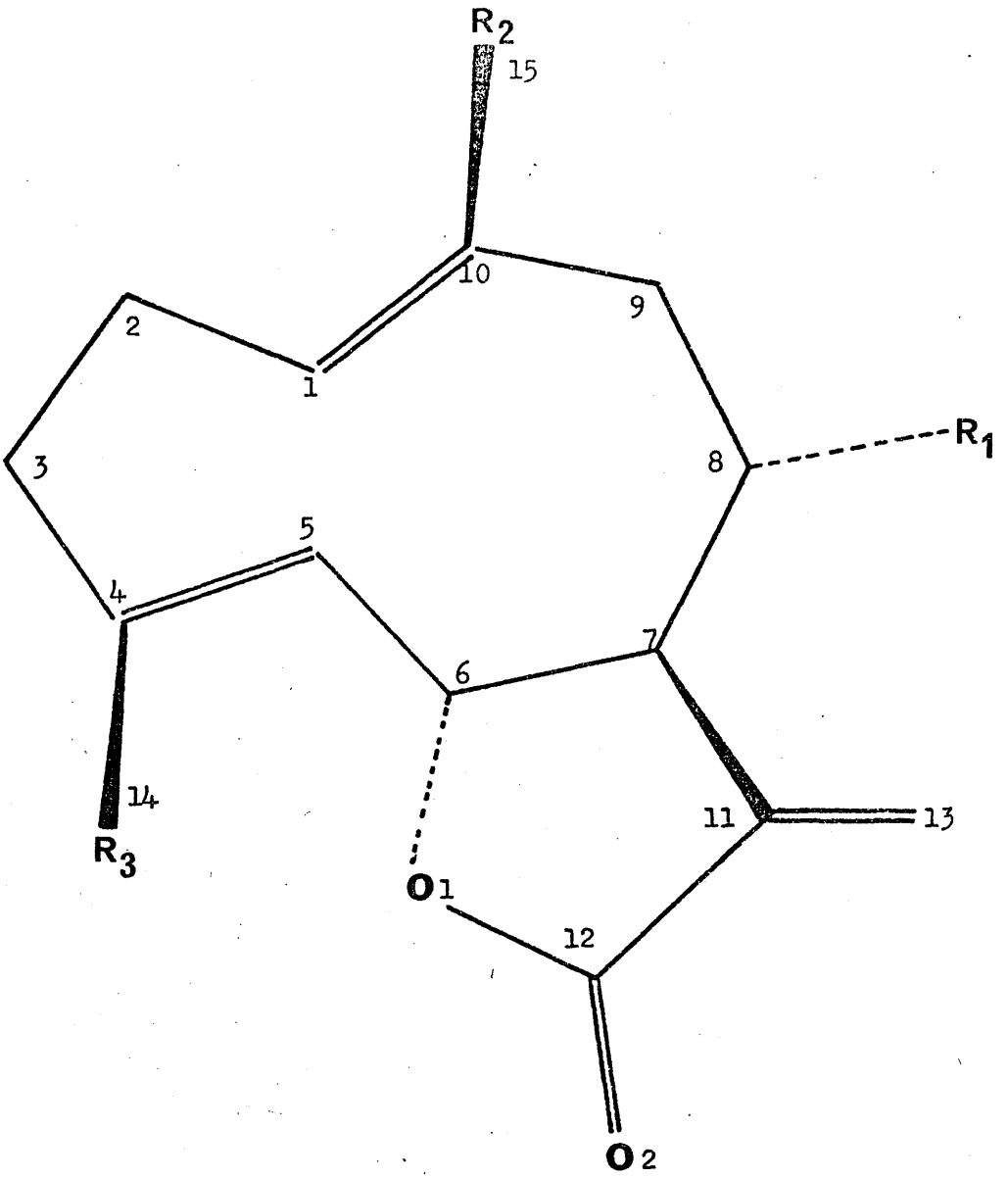

C13
C11
C8
O2
C12
C9
C7
O1
C6
C15
C10
C5
C1
C4
C14
C3
C2

Fig. 2.4 Costunolide crystal packing: A view down the 'c' axis


0 1 2 Å
b
a



	R_1	R_2	R_3
Costunolide	H	CH_3	CH_3
Eupatolide	OH	CH_3	
Alatolide	$OCOCH(CH_3)_2$	CH_2OH	CH_2OH
Eupatoriopicrin	$OCOC(CH_2OH)CHCH_2OH$	CH_3	CH_3
Onopordopicrine	$OCOC(CH_2)CH_2OH$	CH_3	CH_2OH
Jurineolide *	$OCOC(CHCH_2OH)CH_3$	CH_2OH	CH_2OH
Albicolide *	H	CH_2OH	CH_2OH

* No x-ray analysis currently available. Stereochemistry based on ORD/CD observations.

Fig. 2.5 Structure of Costunolide and some related Sesquiterpenoids

TABLE VIII MACROCYCLE TORSION ANGLES IN VARIOUS GERMACRANOLIDES

TORSION ANGLE	COMPOUND					
	CO	EL	AL	ER	ON	FF
1 - 2	-102	-98	-107	-102	-100	-96
2 - 3	52	50	50	50	53	44
3 - 4	-89	-86	-83	-87	-82	-82
4 - 5	156	155	154	154	153	168
5 - 6	-131	-136	-137	-133	-141	-132
6 - 7	89	90	93	90	95	77
7 - 8	-84	-76	-87	-77	-83	-87
8 - 9	74	67	76	66	70	78
9 - 10	-112	-115	-108	-109	-115	-113
10 - 1	164	167	167	166	168	167

CO COSTUNOLIDE
AL ALATOLIDE(12)
ON ONOPORDOPICRINE(14)
EL EUPATOLIDE(11)
ER EUPATORIOPICRIN(13)
FF CALC. DIMETHYL CYCLODECADIENE

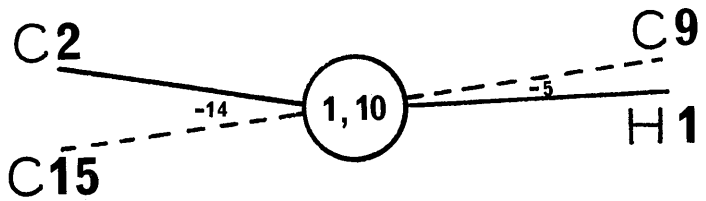
TORSION ANGLES(DEGREES).NUMBERING AS IN FIG. 2.5

TABLE IX MACROCYCLE C-C(SP**3)-C VALENCE ANGLES IN GERMACRANOLIDES

	RANGE	MEAN
COSTUNOLIDE	109 TO 117	113.5
EUPATOLIDE(11)	109 TO 118	114.8
ALATOLIDE(12)	109 TO 115	112.7
EUPATORIOPICRIN(13)	108 TO 119	114.8
ONOPORDOPICRINE(14)	107 TO 129	119.0
PREGEIJERENE(16) *	106 TO 125	118.1
GERMACRATRIENE(17) *	102 TO 116	109.2
ELEPHANTOL(18)	107 TO 124	113.9
DIHYDROMIKANOLIDE(19)	115 TO 122	117.7

ANGLES IN DEGREES

* A GERMACRANE DERIVATIVE CONTAINING NO LACTONE FUNCTION



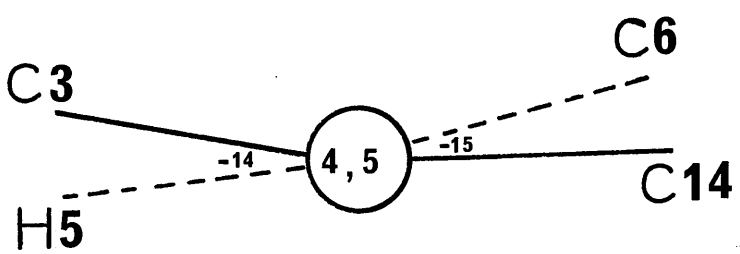


Fig. 2.6 Newman projections down the C(1)-C(10) and C(4)-C(5) bonds of Costunolide

TABLE X THE DISTORTION OF THE CYCLODECADIENE DOUBLE BONDS IN SOME GERMACRANOLIDES

	C(3) - C(4) - C(5) - C(6)				C(9) - C(10) - C(1) - C(2)			
	PHI1	CHI1	CHI2	TOR1	PHI2	CHI3	CHI4	TOR2
COSTUNOLIDE	156.0	-9.1	10.5	165.8	164.5	-1.9	10.5	170.6
EUPATOLIDE(11)	154.9	-8.9	17.7	168.2	166.6	-1.3	14.5	174.5
ALATOLIDE(12)	153.5	-6.1	5.5	174.2	166.6	0.4	25.2	179.0
ONOPORDOPICRINE(14)	153.4	-10.0	12.5	169.7	168.0	-1.9	12.9	175.5
CALCULATED *	168.3	-5.8	5.9	173.5	166.7	-4.3	4.3	173.2

* FOR DIMETHYL CYCLODECADIENE

PHI1 TORSION ANGLE C(3)-C(4)-C(5)-C(6)
PHI2 TORSION ANGLE C(9)-C(10)-C(1)-C(2)

THE FOLLOWING SYMBOLS DESCRIBE THE DISTORTION PARAMETERS OF WINKLER AND DUNITZ(23)

CHI1 OUT OF PLANE BENDING OF C(14)
CHI2 OUT OF PLANE BENDING OF H(5)
CHI3 OUT OF PLANE BENDING OF C(15)
CHI4 OUT OF PLANE BENDING OF H(1)
TOR1 TWIST ABOUT C(4)-C(5)
TOR2 TWIST ABOUT C(10)-C(1)

$\underline{\chi}$ (out of plane) - bending according to the method of Winkler and Dunitz (23). The relative uncertainty of the locations of the hydrogens at C(1) and C(5) prohibits detailed discussion of the values in Table X. It is apparent however that $\underline{\tau}$ and $\underline{\chi}$ are relatively constant from molecule to molecule with $\underline{\chi}$ for the unsubstituted trigonal atoms exhibiting the widest range of values. The deformations at C(4) - C(5) result from almost equal amounts of torsion and out of plane bending while at the other double bond there is virtually no out of plane bending at C(10). The transannular separations C(1)....C(4) and C(1).... C(5) are much shorter (2.8 - 2.9A°) than C(10)....C(4) and C(10)...C(5) (3.2 - 3.4A°) and the van der Waals repulsion between C(1), C(4), C(5) and between their substituents is probably partially relieved by the out of plane bending of H(1), C(14) and H(5) which is in a direction outwards from the ring. The absence of a similar deformation at C(10) may be related to the less crowded environment in the vicinity of this atom.

The C(1) - C(5) trans-annular distance of 2.96A° is very short and this is not unexpected when the separations found for some other germacranes are compared (Table XI). Costunolide shows a UV absorption at 220nm(+ve) (10) and other compounds e.g. jurineolide (10), albicolide (10), have a similar UV band at about 220 nm. It is believed (10, 24) that such absorption at about 200 and 220 nm is the result of a trans-annular interaction between the double bands of the macrocycle giving rise to a $\Pi \rightarrow \Pi^*$ transition and that the sign of the absorption reflects the chirality of the diene. The spectra of costunolide, jurineolide, albicolide, and alatolide are all very

TABLE XI TRANSANNULAR SEPARATION IN SOME GERMACRANOLIDES

	DIST +
COSTUNOLIDE	2.96
EUPATOLIDE(11)	2.94
ALATOLIDE(12)	2.88
EUPATORIOPICRIN(13)	2.94
ONOPORDOPICRINE(14)	2.89
PREGEIJERENE(16)	2.91
ELEPHANTOL(18)	2.98
DIHYDROMIKANOLIDE(19)	3.03
CALCULATED *	2.84

+ C(1)...C(5) TRANSANNULAR SEPARATION IN ANGSTROMS

* FOR DIMETHYL CYCLODECADIENE

similar in this region and this implies that they have identical stereochemistry in the vicinity of the double bonds. The short trans-annular distances, the observed chiral relationship of the double bonds, and the UV spectra all support the case for the postulated intermediate role of germacrane derivatives in biogenesis (1).

The other major feature of the CD spectrum of costunolide (Fig. 2.7) is the negative Cotton effect at 261 nm (7). This has been attributed to the $n \rightarrow \pi^*$ transition of the C=C-C=O system (25, 26). Stöcklin et al (3) have correlated the sign of the absorption with the position and stereochemistry of the lactone ring fusion. In the case of a 6,7 trans-fusion (Fig. 2.3) a negative Cotton effect is predicted in complete agreement with the observed spectrum. Beecham (27) has proposed that there is a relationship between this sign and the C=C-C=O torsion angle Ψ. The value of this angle for costunolide is -10° which, according to Beecham, would give a negative sign. The view has recently been put forward (12) that the C_{α}-C_{β}-C_{γ}-O torsion angle Φ of the α—methylene—γ—lactone may have more relevance. This suggestion is based on the facts that (a) the observed variation in Ψ is large with little apparent effect on the CD spectrum, (b) Ψ and Φ are nearly always in the same sense with the latter usually having greater magnitude, and (c) the more reliable predictive powers of Stöcklin's rule when contrasted with (a)

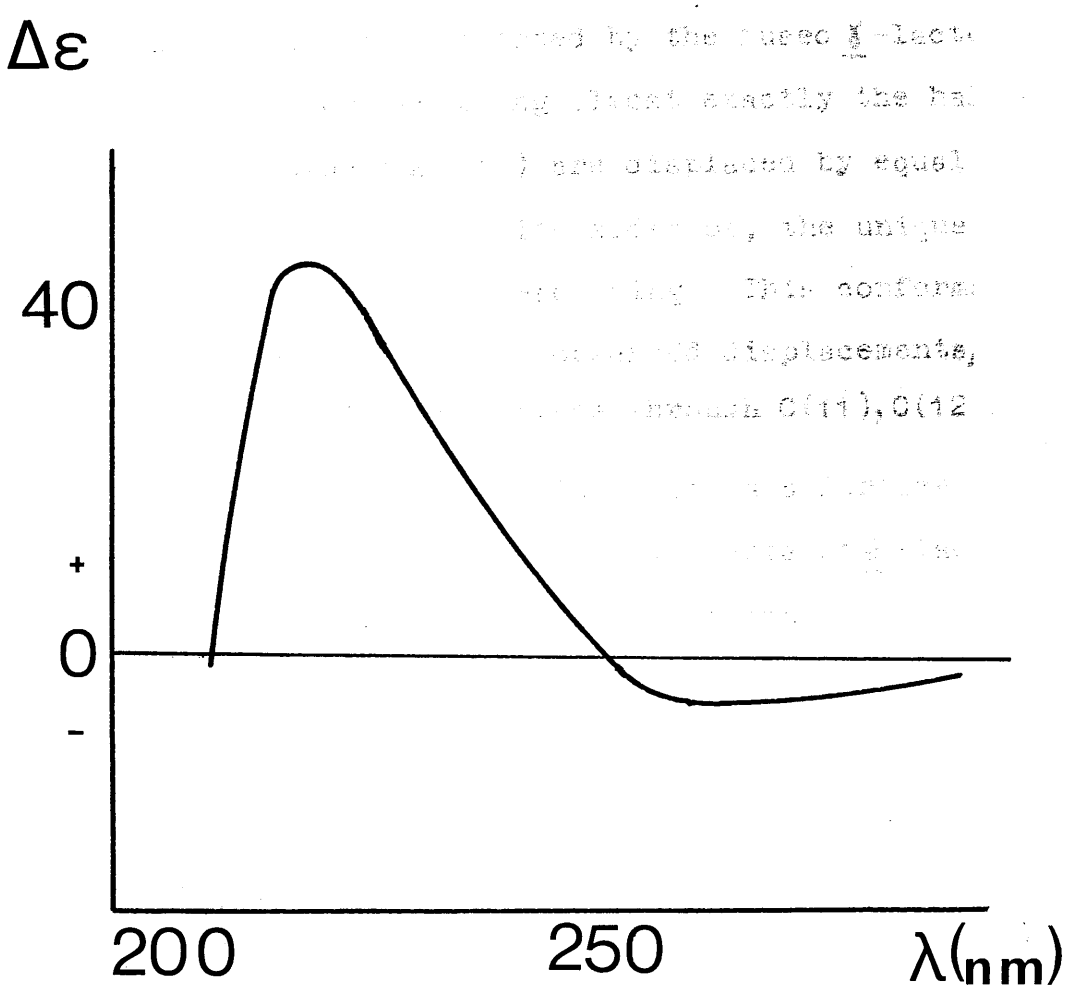


Fig. 2.7 CD spectrum of Costunolide

A quantitative description of the half-chair conformation of the γ-lactone ring was obtained by the method of Cremer and Pople (28). This gave $q = 0.25A^{o}$, $\Phi = 17^{o}$. Since the alternate half-chairs and envelopes assumed by an isolated five-membered ring are separated by phase angles of 18^{o} the conformation adopted by the fused γ-lactone in costunolide is shown as being almost exactly the half-chair in which C(6) and C(7) are displaced by equal amounts ($0.25A^{o}$) from, and to opposite sides of, the unique mean plane through the five membered ring. This conformation is confirmed by the respective observed displacements, 0.212 and $-0.209A^{o}$, from the mean plane through C(11), C(12), O(1).

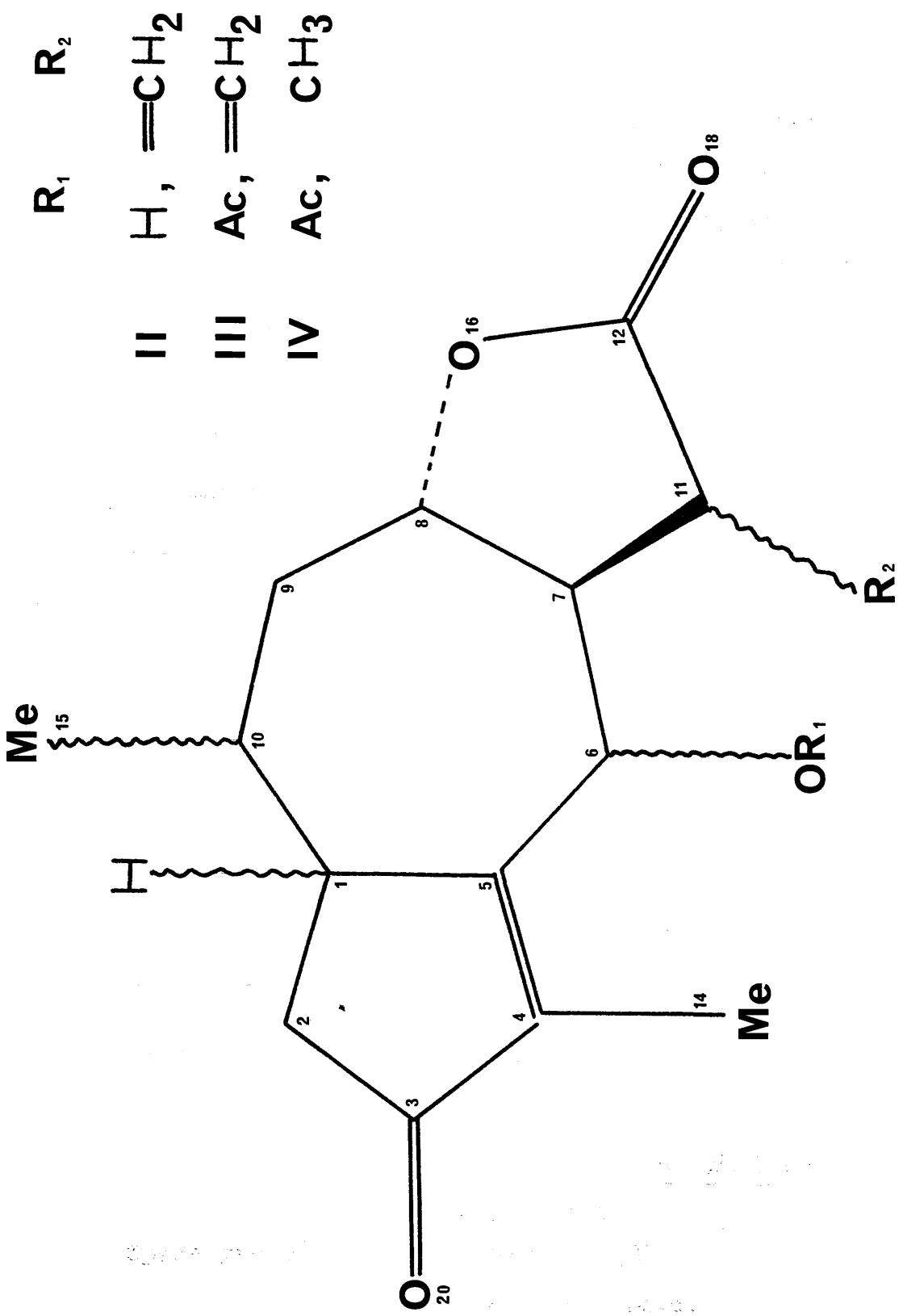
In part II of this thesis there is a further discussion on the stereochemical requirements of γ-lactones on the basis of strain energy calculations.

2.6 Mikanokryptin

Introduction

Mikanokryptin (II) has been extracted from a member of the Mikania species growing in the Canal Zone of Central America (29). The sample used in this analysis was supplied by Professor Herz (Florida State University) who has recently published (29) the results of his structure determination based mainly on spectral observations. Unambiguous assignment of the complete stereochemistry was not possible although comparison of the UV, IR and NMR spectra of related compounds allowed the main structural features to be deduced. The lactone ring

Fig. 2.6a Mikanokryptin and related compounds


R1 R2
II H, =CH2
III Ac, =CH2
IV Ac, CH3
Me
15
10
9
8
O16
12
O18
11
7
R2
6
OR1
1
5
H
2
4
14
Me
3
O20

fusion was elucidated by

(a) application of Samek's rule (30):

$J_{7,13}$ (translactone) $\gtrsim 3 \gtrsim J_{7,13}$ (cislactone)

to the measured chemical shifts of $J_{7,13a}$ = 3.5Hz and $J_{7\,13b}$ = 3.1Hz (13a and 13b represent the two hydrogens attached to C13 (Fig. 2.6a).

(b) the positive sign of the Cotton effect at 257nm (3) in the CD spectrum of acetyl — mikanokryptin (III).

(c) comparison of the physical properties of acetyldihydromikanokryptin (IV) with known cis-fused lactones.

The results of these tests confirmed the trans-fusion of the lactone ring.

The stereochemistry about C(1), C(6) and C(10) remained uncertain and the following x-ray analysis was carried out to determine the complete geometry of the molecule.

2.7 Experimental

Crystal Data

Mikanokryptin $C_{15}H_{18}O_4$

Unit cell dimensions a = 10.366

b = 9.479 $\alpha = \beta = \gamma = 90^{o}$

c = 13.329

Space group $P2_12_12_1$ (D_2^4)

M = 230 a.m.u.

V = 1301 A^{o3}

Do = 1.151 gm cm^{-3}

$Dc = 1.176 \text{ gm cm}^{-3}$

$\mu = 1.03 \text{ cm}^{-1}$ (Mo-Kα_1)

F (ooo)= 560

Z = 4

The systematic absences were:

h00 when h=2n+1, 0k0 when k=2n+1, 00l when l=2n+1.

These defined the space group unambiguously

The crystal used had dimensions 1 x 1 x 1.5 mm.

Data Collection

Cell dimensions and the space group were initially determined from precession photographs. The crystal was then mounted on the goniometer head of the Hilger diffractometer and aligned as described for costunolide. The revised cell dimensions are given in the crystal data. Zirconium filtered Mo-Kα radiation was used to make intensity measurements by means of the θ , 2θ scan procedure.

The following scan parameters being employed:

Increment in θ = 0.02°

No. of scan steps = 40

Time per step = 1 sec.

Immediately before and after each scan the background count was recorded for 20 seconds. Two strong reflexions were monitored as standards during data collection. These standards were checked after every 40 intensity

measurements and showed no significant variation. The intensities of the $\bar{h}\bar{k}\bar{l}$ octant were collected for $2\theta \leq 64^{\circ}$ and placed on a common scale by use of the standards. Integrated intensities (I) were obtained by allowing for the background as described previously. Data for which $I \leq 2\sigma I$ were not included in the subsequent calculations which yielded 2277 independant structure amplitudes.

The data in the range $2\theta \leq 20^{\circ}$ were also collected with reduced beam intensity so that allowance could be made for counter errors.

Structure analysis

The structure was determined by direct phasing using the multisolution program MULTAN. Normalised structure factors were derived and triplet relationships generated for the 400 reflexions with $|E| \geq 1.29$. By accepting phases with a probability in excess of 0.95$ and subsequent convergence mapping the program selected three reflexions to define the origin and enantiomorph.

A further three general reflexions were chosen and the combinations of phases listed in Table XII were used to phase the 400 reflexions. An E-map was calculated from the phase set with the highest combined figure of merit. This E-map revealed all the non-hydrogen atoms.

An initial structure factor calculation gave an R of 35.5% and subsequent least squares calculations using

TABLE XII SUMMARY OF STRUCTURE DETERMINATION

A. INITIAL SET OF PHASES

REFLECTION				PHASE *	MOD. E
6	1	8	+	45 OR 315	2.51
4	4	3	+	45 OR 315	2.41
3	2	2	+	45	2.32
2	4	9		45,135,225 OR 315	2.18
5	0	9		90 OR 270	1.80
0	2	6		0 OR 180	1.70

B. STATISTICS

	E1	E2	E3	E4	E5	E6
THEORETICAL FOR CENTRIC	0.798	1.00	0.968	31.73	4.55	0.27
THEORETICAL FOR ACENTRIC	0.886	1.00	0.736	36.79	1.83	0.01
FOUND	0.900	1.00	0.711	34.02	1.54	0.00

* IN DEGREES
\+ ORIGIN AND ENANTIOMORPH DEFINING

MOD. E MODULUS OF E FOR REFLECTION CONCERNED
E1 MEAN VALUE FOR MODULUS OF E
E2 MEAN VALUE FOR MODULUS OF E**2
E3 MEAN VALUE FOR MODULUS OF ((E**2)-1)
E4 % OF REFLECTIONS WITH MODULUS OF E >1.0
E5 % OF REFLECTIONS WITH MODULUS OF E >2.0
E6 % OF REFLECTIONS WITH MODULUS OF E >3.0

the 2082 reflexions for which $|F_o| \geqslant 3\sigma|F_o|$ with isotropic and then anisotropic thermal parameters reduced $\underline{R}$ to 12.1% . A difference synthesis revealed all the hydrogen atoms. Further least squares calculations with the carbon and oxygen atoms having anisotropic temperature factors and the hydrogen atoms having isotropic temperature factors yielded an $\underline{R}$ of 4.4% . A correction was made for strong reflexions underestimated because of counter saturation, and a weighting scheme of the form:

$$W = 1/(A + BF_o + CF_o^2) \quad \text{with} \quad \begin{array}{l} A = 0.1761 \\ B = -0.0167 \\ C = 0.0018 \end{array}$$

was applied.

The values of the constants were selected so as to minimise the deviation from constant $W\underline{\Delta}^2$ over the range of $|F_o|$ and $\sin\theta$.

The refinement then converged to an $\underline{R}$ of 4.3% . No absorption correction was applied and the ratio of observations to parameters was 8.5 to 1 .

2.8 Results

Table XIII Mikanokryptin: Fractional atomic coordinates

Positional estimated standard deviations are shown in parentheses.

The hydrogen atoms are numbered according to the atoms to which they are attached.

The table shows:

Atom	x	y	z

C(1)	0767(2)	5825(2)	6500(1)
C(2)	0620(2)	6477(3)	7552(1)
C(3)	-0768(2)	6264(2)	7847(1)
C(4)	-1413(2)	5479(2)	7041(1)
C(5)	-0566(2)	5204(2)	6304(1)
C(6)	-0894(2)	4321(2)	5396(1)
C(7)	0269(2)	4063(2)	4715(1)
C(8)	0746(2)	5398(2)	4191(1)
C(9)	1746(2)	6236(2)	4746(2)
C(10)	1234(2)	6921(2)	5714(1)
C(11)	0035(2)	3076(2)	3854(1)
C(12)	0775(2)	3626(2)	2988(1)
C(13)	-0657(3)	1921(3)	3812(2)
C(14)	-2794(2)	5054(3)	7116(2)
C(15)	0217(2)	8043(2)	5495(2)
O(16)	1303(2)	4884(2)	3243(1)
O(18)	0949(2)	3113(2)	2177(1)
O(20)	-1259(2)	6644(2)	8633(1)
O(21)	-1922(1)	4995(2)	4872(1)
H(1)	1429(24)	5063(27)	6509(18)
H(21)	1172(24)	6022(26)	8022(18)
H(22)	0875(29)	7530(31)	7583(22)
H(6)	-1225(21)	3440(24)	5634(17)
H(7)	0963(22)	3644(24)	5156(17)
H(8)	0037(20)	5982(23)	4010(16)
H(91)	2461(24)	5701(26)	4899(18)
H(92)	2054(25)	6984(29)	4297(19)
H(10)	1976(24)	7362(25)	6040(18)
H(131)	-0817(27)	1390(29)	3199(20)
H(132)	-1206(30)	1569(34)	4387(24)
H(141)	-3051(28)	4360(31)	6632(21)
H(142)	-3286(50)	5751(48)	7047(35)
H(143)	-3039(32)	4503(35)	7726(23)
H(151)	-0089(24)	8470(30)	6159(21)
H(152)	0543(32)	8786(33)	5115(23)
H(153)	-0531(28)	7647(31)	5110(21)
H(021)	-2270(29)	4432(30)	4540(22)

Table XIV Mikanokryptin: Thermal parameters

Carbon and oxygen values are anisotropic.

Hydrogen values are isotropic.

Estimated errors in the last two digits are shown in parentheses.

All figures are multiplied by 10^4.

The anisotropic temperature factor expression used was of the form described by equation (12) in chapter one, the coefficients being in terms of the mean square amplitudes of vibration U_{ij} .

The table shows:

Atom U_{11} or U U_{22} U_{33} U_{12} U_{13} U_{23}

C(1)	295(8)	435(10)	281(8)	-55(8)	-18(7)	-9(8)
C(2)	431(12)	592(14)	334(9)	-119(12)	-38(9)	-94(10)
C(3)	450(11)	363(9)	307(9)	-29(10)	-17(9)	-41(8)
C(4)	352(9)	335(9)	289(8)	-47(8)	20(7)	-41(7)
C(5)	322(8)	297(8)	257(7)	-42(7)	-12(7)	4(6)
C(6)	324(8)	318(8)	251(7)	-33(7)	23(7)	-17(7)
C(7)	339(9)	324(9)	256(8)	41(7)	17(7)	9(7)
C(8)	336(9)	378(9)	289(9)	40(8)	45(7)	52(7)
C(9)	311(9)	453(11)	408(10)	-29(9)	53(9)	72(9)
C(10)	317(9)	382(10)	407(10)	-79(8)	5(8)	5(9)
C(11)	442(11)	397(10)	287(9)	92(9)	8(8)	-34(8)
C(12)	465(12)	506(13)	334(10)	167(11)	39(9)	5(10)
C(13)	734(18)	506(14)	510(14)	-79(14)	80(14)	-181(12)
C(14)	386(11)	626(15)	406(11)	-123(12)	104(10)	-105(12)
C(15)	514(14)	365(11)	610(15)	-6(11)	39(12)	6(11)
O(16)	536(9)	546(9)	314(7)	57(9)	137(7)	50(7)
O(18)	754(13)	754(13)	349(8)	145(12)	128(9)	-94(9)
O(20)	639(11)	652(11)	386(9)	-93(12)	101(8)	-218(8)
O(21)	334(7)	556(9)	386(8)	31(8)	-67(6)	-80(7)
H(1)	125(48)					
H(21)	184(61)					
H(22)	279(76)					
H(6)	84(46)					
H(7)	91(49)					
H(8)	65(43)					
H(91)	154(48)					
H(92)	218(50)					
H(10)	158(48)					
H(131)	286(72)					
H(132)	398(90)					
H(141)	290(76)					
H(142)	803(121)					
H(143)	419(73)					
H(151)	269(60)					
H(152)	360(74)					
H(153)	262(66)					
H(021)	287(73)					

TABLE XV

MIKANOKRYPIIN: INTRAMOLECULAR BONDED DISTANCES(ANGSTROMS)
STANDARD DEVIATIONS (ANGSTROMS) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	DIST.	ATOM1	ATOM2	DIST.
C1	C2	1.528(2)	C12	O16	1.353(2)
C1	C5	1.524(2)	C12	O18	1.193(2)
C1	C10	1.550(2)	C1	H1	0.998(23)
C2	C3	1.506(2)	C2	H21	0.947(22)
C3	C4	1.461(2)	C2	H22	1.037(30)
C3	O20	1.213(2)	C6	H6	0.957(21)
C4	C5	1.338(2)	C7	H7	1.009(19)
C4	C14	1.491(2)	C8	H8	0.950(19)
C5	C6	1.504(1)	C9	H91	0.921(21)
C6	C7	1.523(2)	C9	H92	0.980(22)
C6	O21	1.423(2)	C10	H10	0.978(20)
C7	C8	1.526(2)	C13	H131	0.969(24)
C7	C11	1.495(2)	C13	H132	1.006(27)
C8	C9	1.499(2)	C14	H141	0.956(27)
C8	O16	1.466(1)	C14	H142	0.837(42)
C9	C10	1.528(2)	C14	H143	0.997(24)
C10	C15	1.526(3)	C15	H151	1.019(21)
C11	C12	1.475(2)	C15	H152	0.929(28)
C11	C13	1.312(3)	C15	H153	1.001(26)

TABLE XVI MIKANOKRYPTIN: INTERMOLECULAR CONTACTS OF LESS THAN 4.0 ANGSTROMS

ATOM1	ATOM2		DIST #	ATOM1	ATOM2		DIST #
C(3)	O(21)	*	3.800	O(20)	O(21)	*	2.949
C(14)	C(11)	*	3.729	C(11)	C(14)	**	3.942
C(14)	C(12)	*	3.530	C(12)	C(14)	**	3.793
C(14)	C(13)	*	3.988	C(13)	C(14)	**	3.720
C(14)	O(16)	*	3.935	O(18)	C(14)	**	3.406
C(14)	O(18)	*	3.704	C(9)	C(15)	***	3.677
C(14)	O(21)	*	3.686	C(9)	O(21)	***	3.863
O(20)	C(6)	*	3.881	C(10)	O(21)	***	3.579
O(20)	C(11)	*	3.934	C(15)	O(21)	***	3.534
O(20)	C(13)	*	3.482				

IN ANGSTROMS

THE ASTERISKS(*) REFER TO THE FOLLOWING TRANSFORMATIONS OF THE ATOMIC COORDINATES

*	1.5-X, 1.0-Y, 0.5+Z
**	0.5+X, 0.5-Y, 1.0-Z
***	0.5+X, 1.5-Y, 1.0-Z

TABLE XVII

MIKANOKRYPIIN: VALENCY ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ANGLE	ATOM1	ATOM2	ATOM3	ANGLE
C5	C1	C2	102.8(1)	C10	C1	C2	112.0(1)
C10	C1	C5	115.3(1)	C3	C2	C1	106.1(1)
C4	C3	C2	108.3(1)	O20	C3	C2	125.8(1)
O20	C3	C4	125.9(1)	C5	C4	C3	109.4(1)
C14	C4	C3	121.9(1)	C14	C4	C5	128.7(1)
C4	C5	C1	113.2(1)	C6	C5	C1	123.8(1)
C6	C5	C4	123.0(1)	C7	C6	C5	112.6(1)
O21	C6	C5	108.0(1)	O21	C6	C7	112.1(1)
C8	C7	C6	113.1(1)	C11	C7	C6	115.1(1)
C11	C7	C8	102.9(1)	C9	C8	C7	116.1(1)
O16	C8	C7	104.0(1)	O16	C8	C9	109.0(1)
C10	C9	C8	113.3(1)	C15	C10	C1	112.2(1)
C9	C10	C1	112.9(1)	C15	C10	C9	112.2(1)
C13	C11	C7	130.1(1)	C12	C11	C7	106.7(1)
C13	C11	C12	123.2(1)	O16	C12	C11	109.2(1)
O18	C12	C11	129.3(2)	O18	C12	O16	121.5(1)
C12	O16	C8	110.3(1)	H1	C1	C2	110.5(9)
H1	C1	C5	110.2(13)	H1	C1	C10	106.0(11)
H21	C2	C1	110.9(13)	H22	C2	C1	113.6(12)
H21	C2	C3	110.3(14)	H22	C2	C3	111.1(15)
H22	C2	H21	104.9(20)	H6	C6	C7	109.8(12)
H6	C6	O21	106.4(11)	H6	C6	C5	107.7(10)
H7	C7	C8	110.6(12)	H7	C7	C11	108.3(12)
H7	C7	C6	106.8(10)	H8	C8	C9	110.5(12)
H8	C8	O16	106.4(9)	H8	C8	C7	110.3(11)

VALENCE ANGLES (CONTINUED)

ATOM1	ATOM2	ATOM3	ANGLE	ATOM1	ATOM2	ATOM3	ANGLE
H91	C9	C8	111.8(13)	H91	C9	C10	109.3(10)
H92	C9	C10	108.4(13)	H92	C9	C8	108.1(11)
H92	C9	H91	105.6(18)	H10	C10	C15	109.2(13)
H10	C10	C1	103.6(11)	H10	C10	C9	106.2(11)
H131	C13	C11	124.2(16)	H132	C13	C11	123.6(18)
H132	C13	H131	111.6(24)	H143	C14	C4	116.0(16)
H141	C14	C4	114.1(17)	H142	C14	C4	111.4(29)
H142	C14	H141	107.6(30)	H143	C14	H141	96.2(22)
H143	C14	H142	110.3(29)	H153	C15	C10	111.7(16)
H151	C15	C10	109.2(13)	H152	C15	C10	112.3(19)
H152	C15	H151	106.2(22)	H153	C15	H151	110.3(18)
H153	C15	H152	107.0(21)	H021	021	C6	108.4(21)

TABLE XVIII

MIKANOKRYPTIN: TORSION ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
C5	C1	C2	C3	-3.4(1)	C10	C1	C2	C3	121.0(1)
C2	C1	C5	C4	3.6(1)	C2	C1	C5	C6	-174.2(1)
C10	C1	C5	C4	-118.6(1)	C10	C1	C5	C6	63.6(2)
C2	C1	C10	C9	163.9(1)	C2	C1	C10	C15	-68.2(1)
C5	C1	C10	C9	-79.0(1)	C5	C1	C10	C15	48.9(2)
C1	C2	C3	C4	2.4(2)	C1	C2	C3	O20	-179.8(1)
C2	C3	C4	C5	-0.1(2)	C2	C3	C4	C14	178.0(1)
O20	C3	C4	C5	-178.0(1)	O20	C3	C4	C14	0.1(2)
C3	C4	C5	C1	-2.3(1)	C3	C4	C5	C6	175.5(1)
C14	C4	C5	C1	179.8(1)	C14	C4	C5	C6	-2.4(2)
C1	C5	C6	C7	2.5(2)	C1	C5	C6	O21	-121.9(1)
C4	C5	C6	C7	-175.1(1)	C4	C5	C6	O21	60.5(1)
C5	C6	C7	C8	-67.8(1)	C5	C6	C7	C11	174.3(1)
O21	C6	C7	C8	54.2(1)	O21	C6	C7	C11	-63.7(1)
C6	C7	C8	C9	89.9(1)	C6	C7	C8	O16	-150.4(1)
C11	C7	C8	C9	-145.3(1)	C11	C7	C8	O16	-25.6(1)
C6	C7	C11	C12	142.9(1)	C6	C7	C11	C13	-37.9(2)
C8	C7	C11	C12	19.4(1)	C8	C7	C11	C13	-161.4(2)
C7	C8	C9	C10	-67.4(1)	O16	C8	C9	C10	175.6(1)
C7	C8	O16	C12	24.0(1)	C9	C8	O16	C12	148.4(1)
C8	C9	C10	C1	62.2(1)	C8	C9	C10	C15	-65.7(2)
C7	C11	C12	O16	-5.5(2)	C7	C11	C12	O18	173.4(2)
C13	C11	C12	O16	175.2(1)	C13	C11	C12	O18	-5.8(3)
C11	C12	O16	C8	-11.9(2)	O18	C12	O16	C8	169.1(1)
C5	C1	C2	H21	116.4(15)	C5	C1	C2	H22	-125.8(16)
C10	C1	C2	H21	-119.2(15)	C10	C1	C2	H22	-1.4(16)
H1	C1	C2	C3	-121.0(12)	H1	C1	C2	H21	-1.2(19)
H1	C1	C2	H22	116.6(20)	H1	C1	C5	C4	121.5(12)
H1	C1	C5	C6	-56.4(12)	C2	C1	C10	H10	49.4(12)
C5	C1	C10	H10	166.5(12)	H1	C1	C10	C9	43.3(12)

TORSION ANGLES (CONTINUED)

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
H1	C1	C10	C15	171.2(12)	H1	C1	C10	H10	-71.2(17)
H21	C2	C3	C4	-117.9(15)	H21	C2	C3	O20	60.0(15)
H22	C2	C3	C4	126.2(15)	H22	C2	C3	O20	-55.9(16)
C3	C4	C14	H141	-165.3(18)	C3	C4	C14	H142	72.5(28)
C3	C4	C14	H143	-54.8(17)	C5	C4	C14	H141	12.4(18)
C5	C4	C14	H142	-109.8(28)	C5	C4	C14	H143	122.9(17)
C1	C5	C6	H6	123.6(12)	C4	C5	C6	H6	-54.0(12)
C5	C6	C7	H7	54.1(12)	O21	C6	C7	H7	176.1(12)
H6	C6	C7	C8	172.3(12)	H6	C6	C7	C11	54.4(12)
H6	C6	C7	H7	-65.8(17)	C5	C6	O21	H021	-158.3(20)
C7	C6	O21	H021	77.1(20)	H6	C6	O21	H021	-42.9(24)
C6	C7	C8	H8	-36.7(11)	C11	C7	C8	H8	88.1(11)
H7	C7	C8	C9	-29.9(12)	H7	C7	C8	O16	89.8(12)
H7	C7	C8	H8	-156.4(17)	H7	C7	C11	C12	-97.7(12)
H7	C7	C11	C13	81.4(12)	C7	C8	C9	H91	56.6(13)
C7	C8	C9	H92	172.4(13)	O16	C8	C9	H91	-60.3(13)
O16	C8	C9	H92	55.5(13)	H8	C8	C9	C10	59.1(11)
H8	C8	C9	H91	-176.9(18)	H8	C8	C9	H92	-61.1(17)
H8	C8	O16	C12	-92.5(11)	C8	C9	C10	H10	175.1(12)
H91	C9	C10	C1	-63.2(13)	H91	C9	C10	C15	168.8(13)
H91	C9	C10	H10	49.6(18)	H92	C9	C10	C1	-177.8(13)
H92	C9	C10	C15	54.3(13)	H92	C9	C10	H10	-65.0(18)
C1	C10	C15	H151	52.1(13)	C1	C10	C15	H152	169.6(18)
C1	C10	C15	H153	-70.2(15)	C9	C10	C15	H151	-179.7(13)
C9	C10	C15	H152	-62.2(18)	C9	C10	C15	H153	58.0(15)
H10	C10	C15	H151	-62.2(18)	H10	C10	C15	H152	55.3(22)
H10	C10	C15	H153	175.5(20)	C7	C11	C13	H131	174.2(19)
C7	C11	C13	H132	4.6(20)	C12	C11	C13	H131	-6.8(19)

THE ANGLE 1-2-3-4 IS DEFINED AS POSITIVE IF, WHEN VIEWED ALONG THE 2-3 BOND, ATOM 1 HAS TO BE ROTATED CLOCKWISE TO ECLIPSE ATOM 4

TABLE XIX MIKANOKRYPTIN: MEAN PLANES CALCULATIONS

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
1.	C(1)		-0.007(2)
	C(2)		0.012(3)
	C(3)		-0.012(2)
	C(4)		-0.008(2)
		C(5)	0.041(2)
		C(14)	0.035(3)
		O(20)	-0.010(2)
2.	C(1)		-0.020(2)
	C(2)		0.017(3)
	C(3)		-0.008(2)
	C(4)		-0.006(2)
	C(5)		0.017(2)
		C(14)	0.015(3)
		O(20)	0.006(2)
3.	C(2)		0.000(2)
	C(3)		0.000(2)
	C(4)		0.000(3)
		O(20)	0.033(2)
4.	C(3)		0.000(2)
	C(4)		0.000(2)
	C(5)		0.000(2)
		C(14)	-0.043(3)

TABLE XIX (CONTINUED)

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
5.	C(4)		0.000(2)
	C(5)		0.000(2)
	C(6)		0.000(2)
		C(14)	0.048(3)
6.	C(1)		0.000(2)
	C(5)		0.000(2)
	C(4)		0.000(2)
		C(14)	-0.003(3)
7.	C(11)		0.000(2)
	C(12)		0.000(2)
	O(16)		0.000(2)
		C(7)	0.139(2)
		C(8)	-0.282(2)
		C(13)	-0.092(3)
		O(18)	0.018(2)
8.	C(7)		0.000(2)
	C(11)		0.000(2)
	C(12)		0.000(2)
		C(8)	0.495(2)
		C(13)	-0.015(3)
		O(16)	0.124(2)
		O(18)	-0.107(2)

TABLE XIX (CONTINUED)

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
9.	C(7)		-0.018(2)
	C(11)		0.029(2)
	C(12)		-0.031(2)
	O(16)		0.020(2)
		C(8)	0.394(2)
		C(13)	0.091(3)
		O(18)	-0.128(2)
10.	C(11)		-0.002(2)
	C(12)		0.006(2)
	O(16)		-0.002(2)
	O(18)		-0.002(2)
		C(7)	-0.153(2)
		C(8)	0.269(2)
		C(13)	0.095(3)
11.	C(13)		0.000(3)
	H(131)		0.000(28)
	H(132)		0.000(32)
		C(11)	0.177(2)

Table XIX (continued)

The out of plane atoms were not included in the derivation of the planes. The equations of these planes are:

1. $0.2548x - 0.8689y + 0.4244z = 1.7314$
2. $0.2578x - 0.8627y + 0.4351z = 1.9044$
3. $0.2427x - 0.8616y + 0.4458z = 1.8698$
4. $-0.2430x + 0.8616y - 0.4456z = -1.8707$
5. $-0.2982x + 0.8224y - 0.4846z = -2.9317$
6. $0.2708x - 0.8426y + 0.4655z = 2.4037$
7. $0.8182x - 0.4698y + 0.3314z = 8.8434$
8. $-0.7901x + 0.5461y - 0.2784z = -8.0568$
9. $-0.8239x + 0.4947y - 0.2716z = -8.5435$
10. $-0.8157x + 0.4657y - 0.3389z = -8.8849$
11. $-0.7198x + 0.6464y - 0.2592z = -7.0786$

2.9 Discussion of results

Tables XIII - XIX[++] summarise the results of the x-ray analysis. A view of the molecule is given in Fig. 2.8 and the crystal packing viewed along the b axis is illustrated

++ The torsion angles in Table XVIII give the enantiomer and the signs should therefore be reversed to obtain the correct absolute stereochemistry.

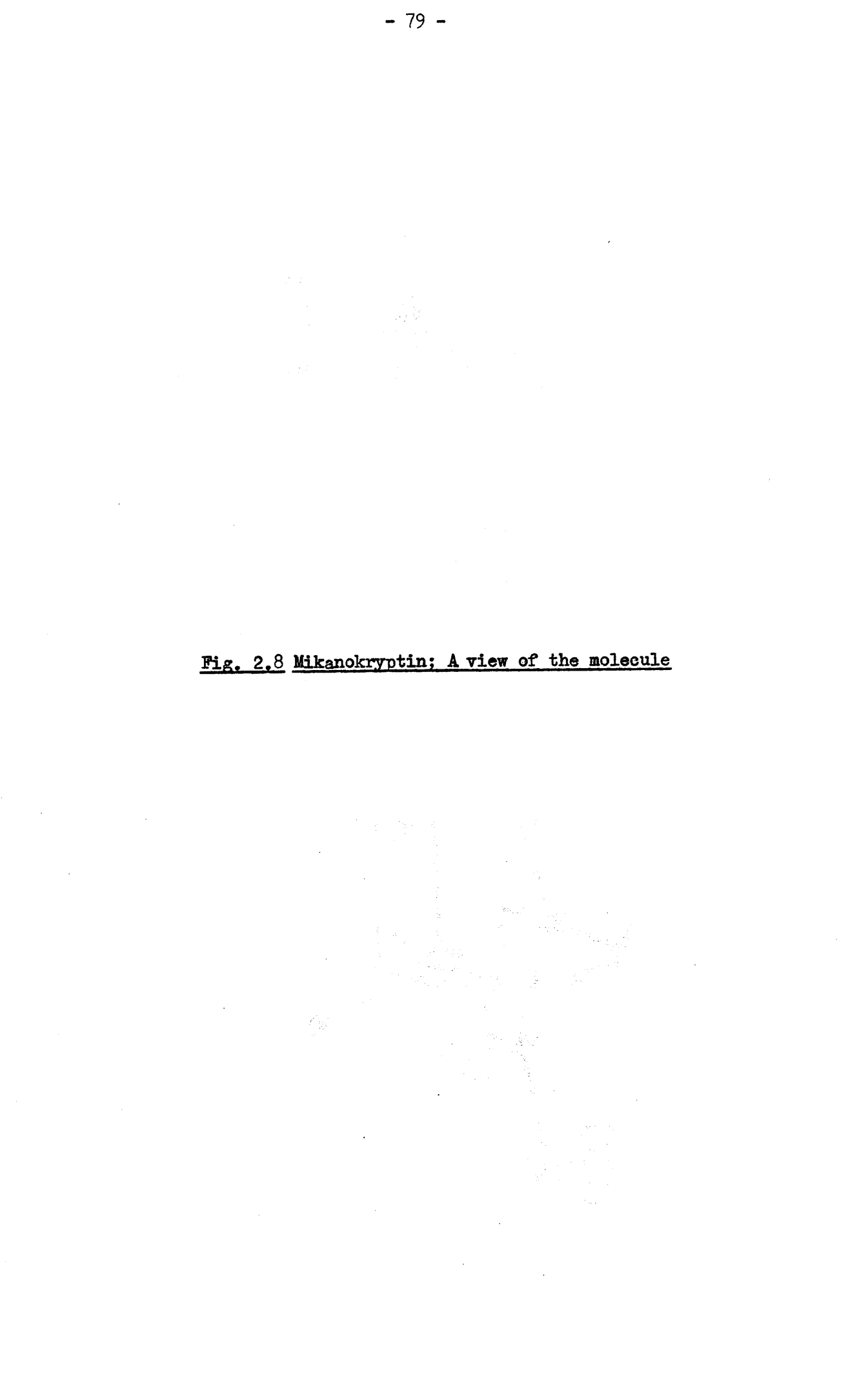


Fig. 2.8 Mikanokryptin; A view of the molecule

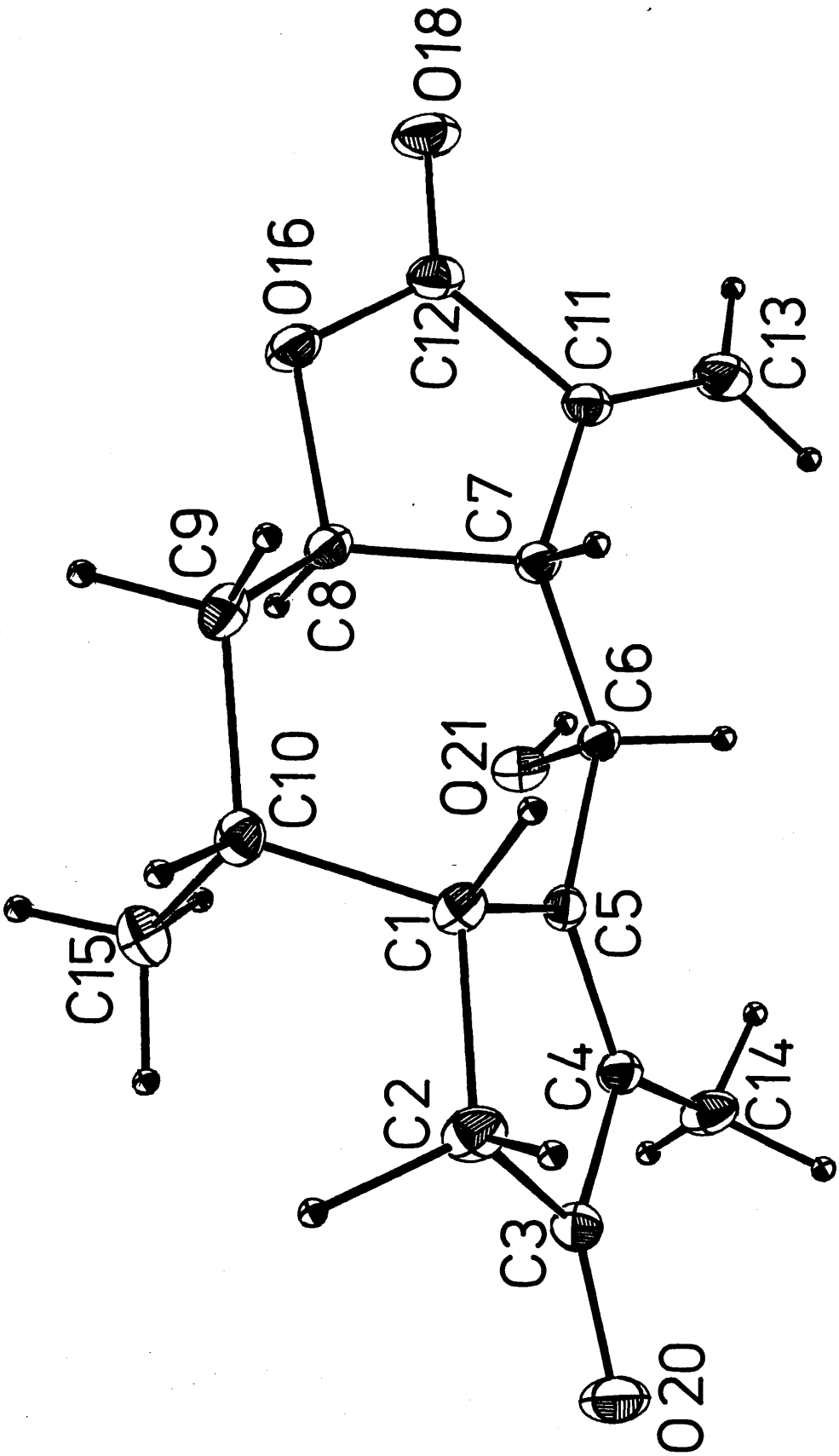
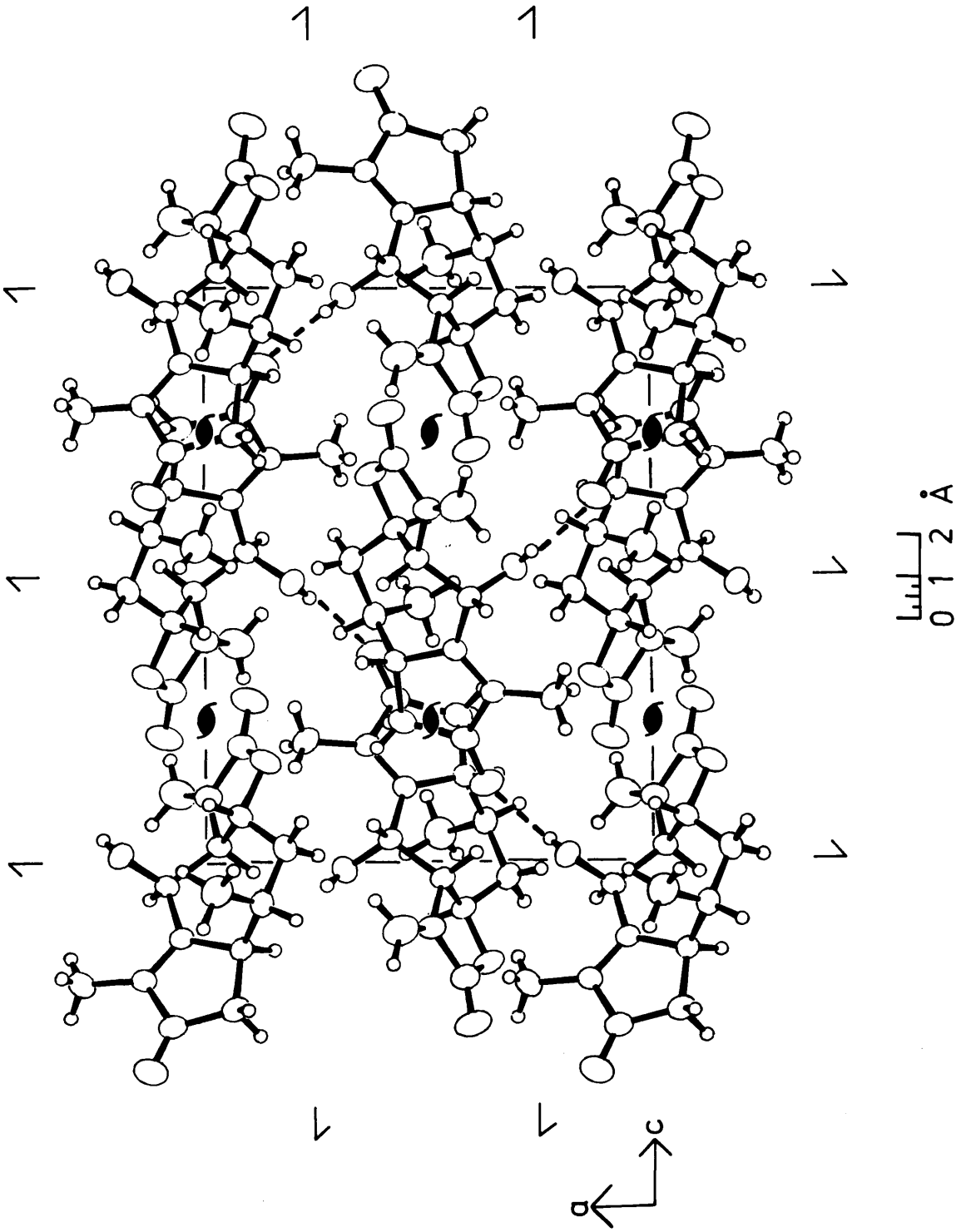

O18
O16
C12
C11
C13
C9
C7
C8
C6
C10
O21
C15
C1
C5
C2
C4
C14
C3
O20

Fig. 2.9 Mikanokryptin crystal packing: A view down the 'b' axis


1
1
1
1
1
1
1
1
0 1 2 Å
a
c

in Fig. 2.9 . The final and observed structure factors are listed in Table XXII.

The stereochemistry of mikanokryptin was established as shown in Fig. 2.10 . The absolute configuration was not determined, but if it is assumed that the C(7) side chain is $\underline{\beta}$, as in almost all sesquiterpene lactones*, then the relative orientations of the asymmetric centres are in agreement with the predictions of Herz et al (29). That is, for example, H(1) $\underline{\alpha}$, C(6) hydroxyl $\underline{\beta}$, and C(10) methyl $\underline{\beta}$,

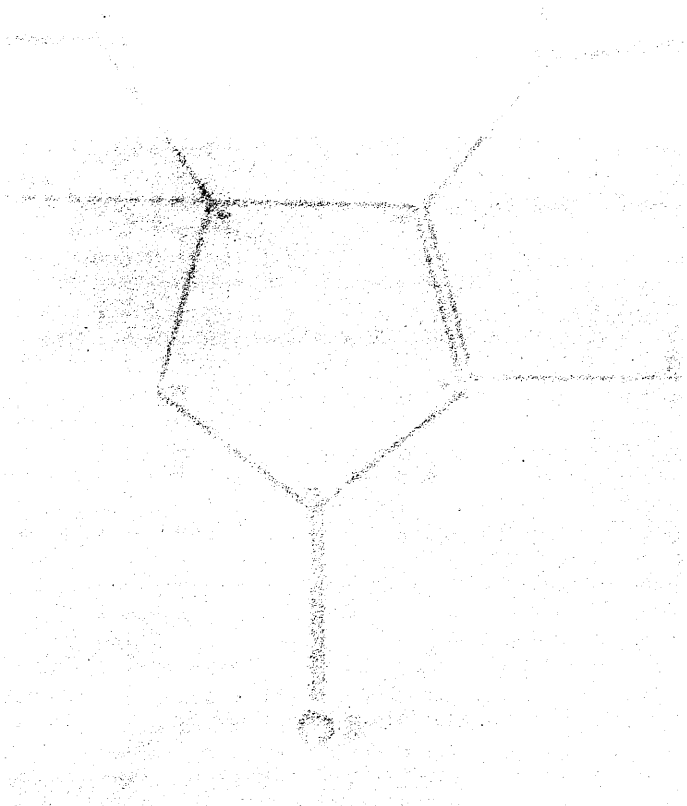
Intermolecular hydrogen bonding occurs between the carbonyl O(20) in one molecule and the C(6) hydroxyl function in another (Table XVI). The oxygen atoms are separated by 2.95Å and the H(021)....O(20) distance is 2.20Å. These three atoms are situated so as to form an O(20)....H(021) - O(21) angle of 162° .

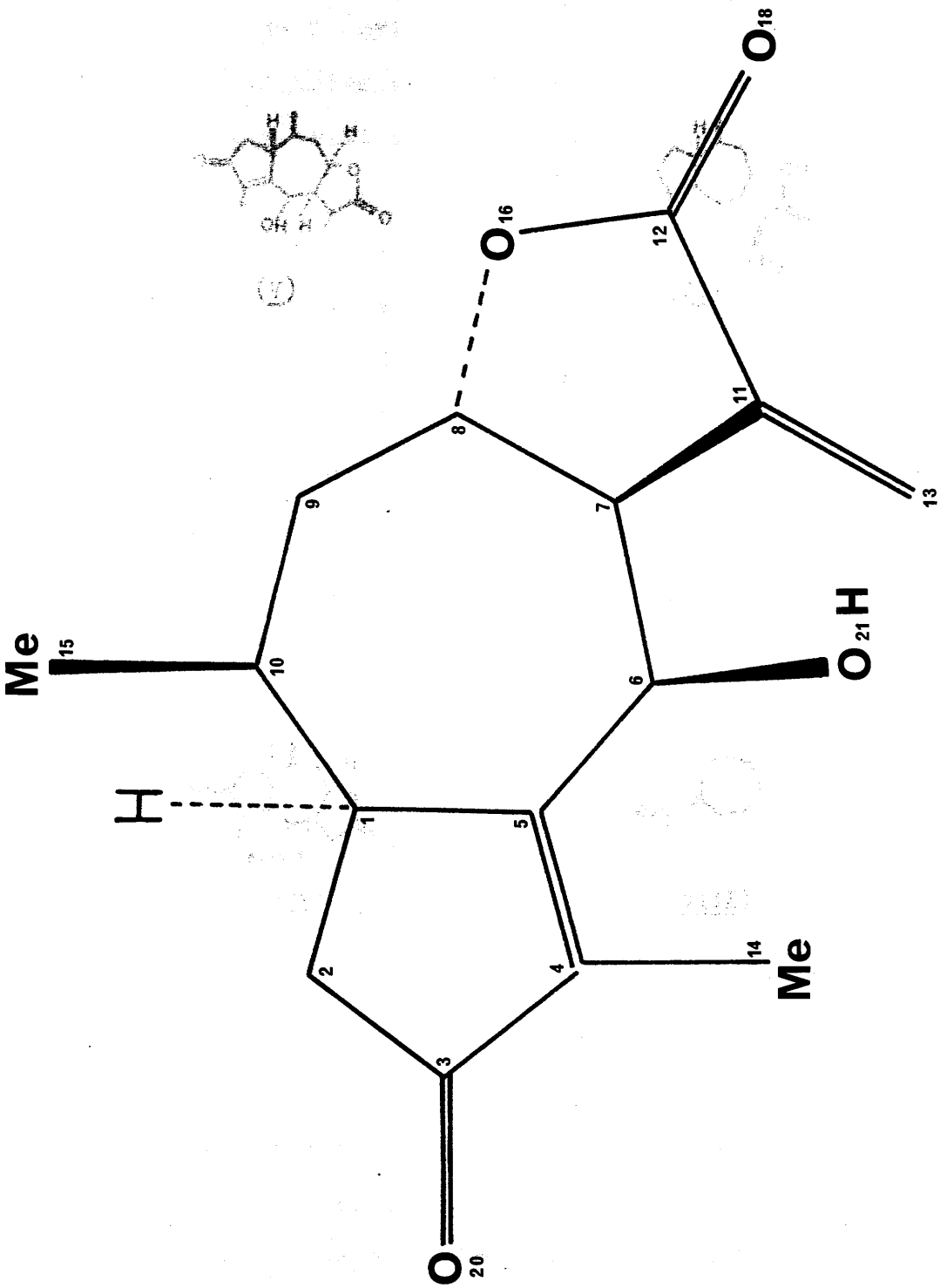
Mikanokryptin has the unusual structural feature of an sp^2 carbon atom at one of the points of fusion of the five and seven membered carbocycles and only a small number of similar guianolides has been studied. Both geigerin (V) and some of its analogues (31,32) and aciphyllic acid (VI) (33) have been examined by spectral techniques, while the only corresponding crystal structure analysis in the literature is the report (34) on bromogeigerin (VII).

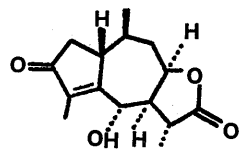
However, calculations (35,36,37,38) have been carried out for isolated cycloheptanes and cycloheptenes and x-ray

* An exception is Centurepensin, a naturally occurring guianolide containing chlorine. See: A. T. Hewson, R. C. Pettersen, and O. Kennard, Cryst. Struct. Comm; 1, 383, (1972) .

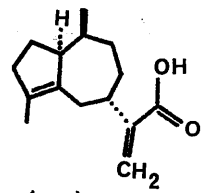
Fig. 2.10 Structure of Mikanokryptin



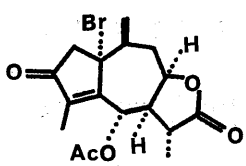

O18
O16
12
11
8
9
7
13
Me
15
10
6
O21H
H
1
5
2
4
14
Me
3
O20



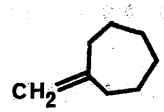
(V)



(VI)



(VII)

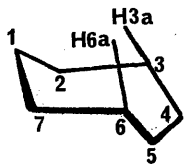


(VIII)

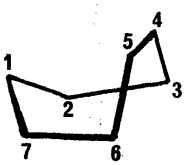
results are available for some guianolides (e.g. 39,40,41) containing these systems.

It is well known that both cycloheptane and cycloheptene can exist in families of chairs and boats (Fig. 2.11). In the cycloalkane there is a $\underline{C}_2$ and $\underline{C}s$ form within each family, with the former being the most stable. In the $\underline{C}s$ conformers, chairs are preferred to boats by 1.0 to 2.5 K.cal(35). The twist chairs are more stable than the chairs mainly because of a strong H(3a)....H(6a) transannular interaction in the latter (Fig. 2.11), which is relieved by pseudorotation to a twist form. The cycloalkene presents a slightly different situation in that the two sp^2 carbon atoms, with normal valence angles of 120°, facilitate an increase in the H(3a) ....H(6a) separation and most workers agree (36,37,38) that the $\underline{C}_2$ twist conformations are just slightly less stable than those possessing a plane of symmetry. This is supported by the fact that spectroscopic studies have found a preference for cycloheptene to exist in the chair form (42,43).

The cycloheptane ring in mikanokryptin represents a situation somewhere between cycloheptane and cycloheptene and as a suitable force field was available (44, Appendix A), it was decided to calculate minimum energies and geometries for the twist chair and chair for 1-methylidene cycloheptane (VIII). The boat family was not included in the calculation since this is generally accepted to be less stable. The force field was also used for calculations of the $\underline{C}_2$ and $\underline{C}_s$ chairs of cycloheptane and cycloheptene so that these results could be correlated with the data already published (Table XX).

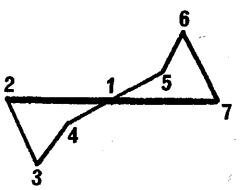


C_s

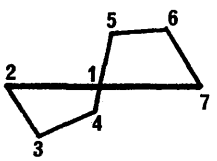


Chair

Boat



C_2



Twist-chair

Twist-boat

Similar conformations exist for cycloheptene

Fig. 2.11 Major conformers of cycloheptane

TABLE XX CONFORMATIONS AND ENERGIES OF VARIOUS SEVEN MEMBERED RINGS

	CYCLOHEPTANE				CYCLOHEPTENE				VIII		
OMEGA	CHAIR		T.CHAIR		CHAIR		T.CHAIR		CH	TC	MK
	HE	TH	HE	TH	ER	TH	ER	TH	TH	TH	CR
1	-70	-65	-76	-74	-68	-70	-28	-32	-65	-70	-67
2	92	85	97	86	75	75	78	79	84	86	90
3	-71	-67	-41	-38	-59	-58	-43	-43	-67	-44	-68
4	0	0	-41	-38	0	0	-43	-43	1	-33	3
5	71	67	97	86	59	58	78	79	65	84	63
6	-92	-85	-76	-74	-75	-75	-28	-32	-84	-77	-79
7	70	65	53	58	68	70	-8	-2	66	59	62
SIG2	114	105	0	0	92	90	0	0	108	19	104
SIGS	0	0	141	114	0	0	154	160	4	93	24
QUOT	1.00	1.00	---	---	1.00	1.00	---	---	0.96	0.17	0.81
ENERGY											
HE	2.16		0.00								
ER					0.00		0.42				
FA					0.00		1.71				
AL					0.00		0.57				
TH	0.74		0.00		0.00		1.53		0.00	0.94	

ENERGIES(K.CAL/MOLE) ARE QUOTED RELATIVE TO THE MOST STABLE ISOMER IN EACH SET OF CALCULATIONS

SYMBOLS EXPLAINED ON FOLLOWING PAGE

EXPLANATION OF SYMBOLS IN TABLE XX

HE	HENDRICKSON(35)
ER	ERMER(38)
FA	FAVINI(36)
AL	ALLINGER(37)
TH	CALCULATIONS REPORTED IN THIS THESIS
OMEGA	TORSION ANGLES IN SEVEN MEMBERED RING AS SHOWN IN FIG.2.12
SIG2	SEE FIG.2.12 FOR EXPLANATION
SIGS	SEE FIG.2.12 FOR EXPLANATION
QUOT	SEE FIG.2.12 FOR EXPLANATION
CH	CHAIR CONFORMATION
T.CHAIR	TWIST CHAIR CONFORMATION
TC	TWIST CHAIR CONFORMATION
MK/CR	MIKANOKRYPTIN CRYSTAL STRUCTURE

These results confirm the relative values obtained by Hendrickson (35) for the chair and twist chair of cycloheptane, the latter conformation being more stable by 0.74 K.cal per mole (Hendrickson 2.16 K.cal per mole).

In cycloheptene the calculations of Favini (36), Allinger (37), and Ermer (38) predicted a preference for the Cs over the C_2 form and a similar relationship has been produced in this work. Although the enthalpy difference of 1.5 K.cal per mole is somewhat larger than those of Allinger (0.57) and Ermer (0.42) the geometry is very similar to that computed by Ermer, and the agreement with the experimental data, that, for most derivatives the chair is preferred by about 1-2 K.cal per mole (45), is good.

Thus the calculated values for the geometries and energies of cycloheptane and cycloheptene are consistent with those of other workers. Similar calculations for VIII indicated that the most stable conformation corresponds more closely to Cs than C_2 symmetry.

In mikanokryptin the carbocycle corresponding to VIII adopts a chair conformation in contrast to the more frequently observed twist chair in the cycloheptane rings of guianolides. The chair conformation is most common when the guianolide structure contains a cycloheptene system as shown in Table XXI.

In this table the torsion angles ω_1 to ω_7 are arranged so that the Cs plane in the chair conformations and the C_2

TABLE XXI CONFORMATION OF THE SEVEN MEMBERED RING IN VARIOUS GUIANOLIDES

	CYCLOHEPTANES					=#		=##		CYCLOHEPTENES			
OMEGA	EB	BS	BH	BM	OH	SO	IF	BG	MK	BL	DG	BL	CL
1	-49	-72	61	51	-76	-69	-59	-69	67	-93	-66	-57	33
2	85	81	-98	-86	87	92	80	90	-90	69	76	76	-76
3	-42	-42	53	60	-51	-45	-68	-43	68	-30	-61	-73	28
4	-41	-31	32	19	-23	-35	3	-37	-3	-1	4	6	49
5	102	79	-81	-82	65	88	68	84	-63	29	60	64	-78
6	-63	-78	59	68	-64	-74	-87	-59	79	-52	-85	-82	22
7	25	63	36	-36	65	51	62	44	-62	74	69	64	11
FUSN	CT*	CT*	TC	CC	TC	CT*	TC	-C	-T	-T	TT	TT*	-C
SIG2	32	19	40	62	62	19	101	22	104	110	92	116	34
SIGS	147	80	154	74	71	114	13	134	24	38	17	28	197
QUOT	0.18	0.19	0.21	0.46	0.47	0.14	0.89	0.14	0.81	0.74	0.84	0.80	0.17

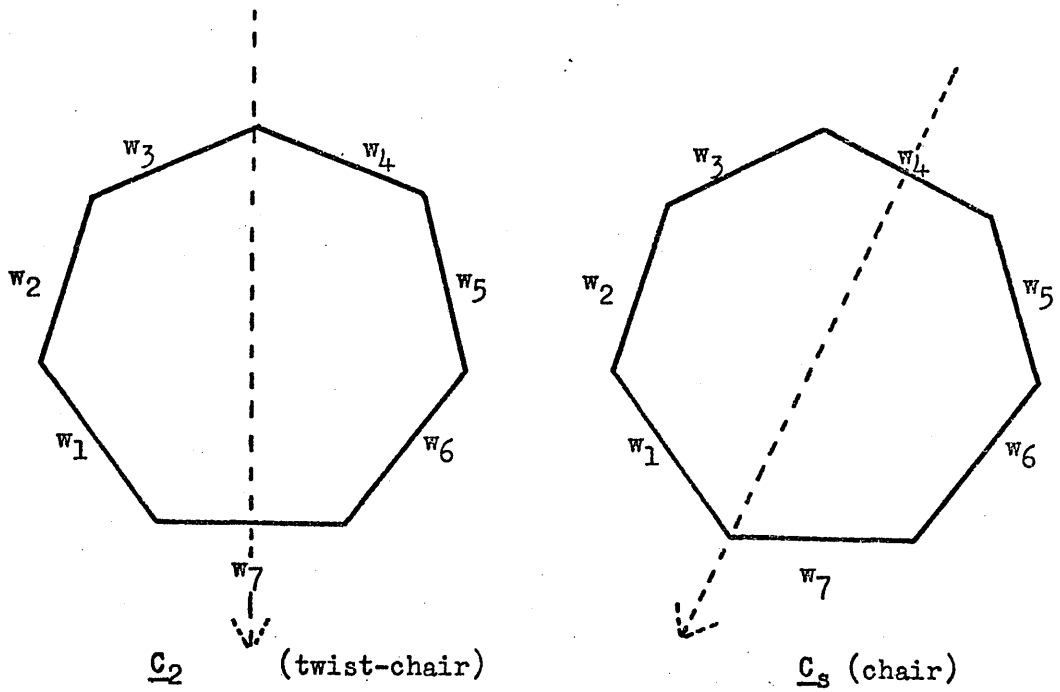
SYMBOLS EXPLAINED ON FOLLOWING PAGE

EXPLANATION OF SYMBOLS IN TABLE XXI

EB	EUPAROTIN BROMOACETATE(40)
BS	BROMODIHYDROISOPHOTOSANTONIC LACTONE ACETATE(46)
BH	BROMOHELANIN(47)
BM	BROMOMEXICANIN-E(48)
OH	AN OXIDE OF HELANIN(49)
SO	SOLISTAN(50)
IF	4-ACETYL-2-P-IODOBENZOYLFLORILENALIN(51)
BG	BROMOGEIGERIN(34)
MK	MIKANOKRYPTIN (TORSION ANGLES HAVE OPPOSITE SIGNS TO THOSE IN TABLE XVIII,TO GIVE CORRECT ABSOLUTE CONFIGURATION)
BL	BROMOGAILLARDIN(39)
DG	DEACETYLDIHYDROGAILLARDIN P-BROMOBENZOATE(39)
BL	BERLANDIN(41)
CL	CAROLENALONE(52)
=#	SEVEN MEMBERED RING INCORPORATES AN EXOCYCLIC DOUBLE BOND WHICH IS NOT LOCATED AT ONE OF THE POINTS OF FUSION TO THE CYCLOPENTANE/ENE
=##	SEVEN MEMBERED RING INCORPORATES AN EXOCYCLIC DOUBLE BOND WHICH IS LOCATED AT ONE OF THE POINTS OF FUSION TO THE CYCLOPENTANE/ENE
OMEGA	TORSION ANGLES IN SEVEN MEMBERED RING AS SHOWN IN FIG.2.12
FUSN	STEREOCHEMISTRY OF RING FUSIONS IN THE ORDER CYCLOPENTANE/ENE,LACTONE. THE SYMBOLS C,T REPRESENT CIS,TRANS RESPECTIVELY. THE SYMBOL '-' REPRESENTS A FUSION IN WHICH THERE IS AN (SP**2) CARBON ATOM AT ONE OF THE RING JUNCTIONS.
*	THESE LACTONES ARE 6,7 FUSED. ALL OTHERS ARE 7,8
SIG2	SEE FIG.2.12 FOR EXPLANATION
SIG3	SEE FIG.2.12 FOR EXPLANATION
QUOT	SEE FIG.2.12 FOR EXPLANATION

axis in the twist forms are located as described by McPhail and Sim (40) and illustrated in Fig. 2.12 which also gives their algorithm for calculating the deviations from absolute Cs or C_2 symmetry.

Table XXI shows quite clearly that there is a wide range of possible conformations in the C-7 ring of guianolides. Only the chair and twist chair variants have been considered in this compilation, but boat-like stereochemistry is also known(53). The conformation adopted is probably influenced by the requirements of the modes of fusion of the two five membered rings. In compounds I to V in Table XXI for instance three different permutations are apparent. Euparotin bromoacetate (EB) and bromodihydroisophotosantonic lactone acetate (BS) have almost identical values of the function $\Sigma_2/(\Sigma_2+\Sigma_s)$ and thus both seven membered rings are closer to twist chairs than chairs although the chair form of cycloheptane would apparently require less distortion to produce the stereochemistry observed in the vicinity of the ring fusions than the twist chair (Fig. 2.13). However, the calculations have shown that for an isolated cycloheptane the C_2 form is more stable and because of the predominance of this conformation in the guianolides incorporating a cycloheptane ring it would appear that the minimum energy conformation of the isolated ring is adopted if at all possible. The torsion angles in this ring for euparotin bromoacetate correspond most closely to the twist chair and Figure (2.13) illustrates that the calculated minimum energy twist chair would permit cis fusion of the cyclopentene ring (with an observed C4-C5-C1-C2 angle of $+18^{\circ}$) more readily than the corresponding transfusion and the



w_1 to w_7 are the respective endocyclic torsion angles

$$\Sigma_2 = (|w_1-w_6| + |w_2-w_5| + |w_3-w_4|)$$

$$\Sigma_s = (|w_1+w_7| + |w_2+w_6| + |w_3+w_5| + |w_4|)$$

$$QUOT = \Sigma_2 / (\Sigma_2 + \Sigma_s)$$

QUOT

approaches 1.0 for conformations close to chair

approaches 0.0 for conformations close to twist-chair

Fig. 2.12 Relationships between cycloheptane torsion angles and conformation(40)

Fig. 2.13 Euparotin Bromoacetate: Stereochemistry in the vicinty of the ring fusions.

(a) - (d) Newman projections down the C(5)-C(1) and C(6)-C(7) bonds of the calculated chair and twist-chair of cycloheptane (FFI).

(a) Twist-chair down C(5)-C(1)

(b) Chair down C(5)-C(1)

(c) Twist-chair down C(6)-C(7)

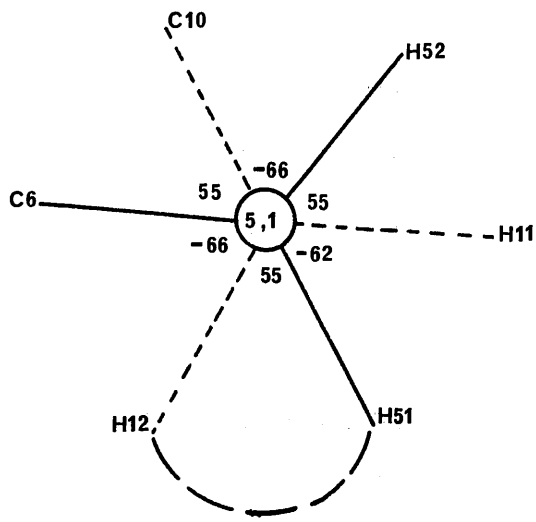
(d) Chair down C(6)-C(7)

Torsion angles are quoted in degrees and the (longer) dashed lines indicate the points of fusion which would produce the correct stereochemistry.

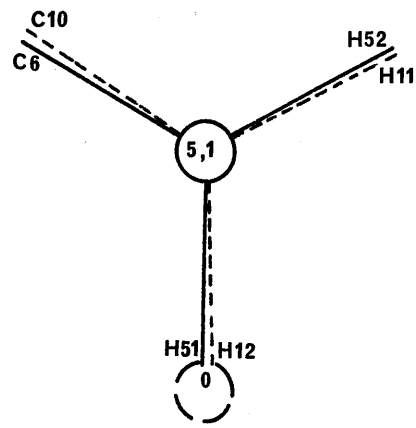
(e) Location of the C_2 axis in the crystal structure of this compound and relationship to the torsion angles (w_1 to w_7) used in Tables XX andXXI.

(f) Correlation between the locations preferred for fusion to an isolated cycloheptane as reported by Hendrickson(35) and the torsion angles w_1 to w_7 .

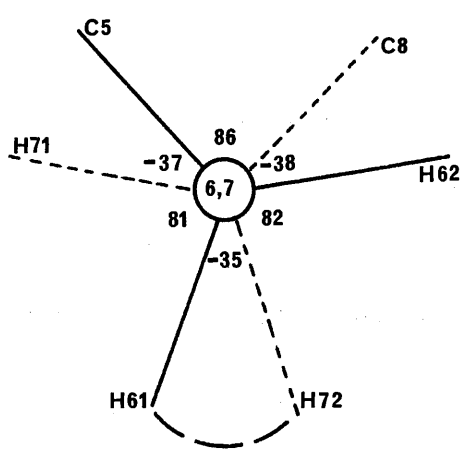
(a)


C10
H52
-66
C6
55
55
5,1
H11
-66
-62
55
H12
H51

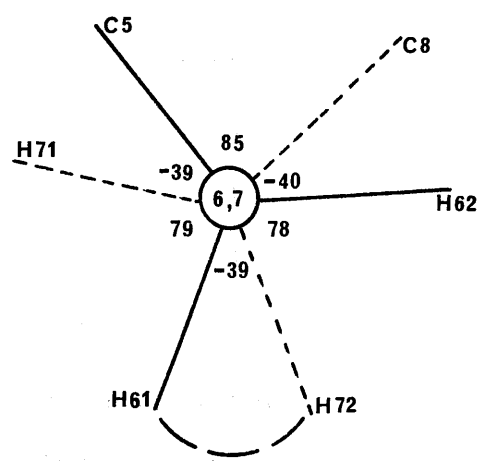
(b)

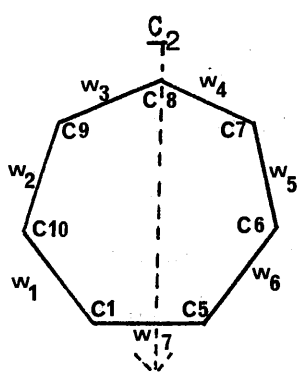

C10
C6
H52
H11
5,1
H51
H12
0

(c)

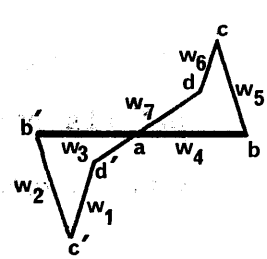

C5
C8
H71
86
-37
-38
H62
6,7
81
82
-35
H61
H72

(d)


C5
C8
H71
85
-39
-40
H62
6,7
79
78
-39
H61
H72


C2
w3
C8
w4
C9
C7
w2
w5
C10
C6
w1
w6
C1
C5
w7

(e)


c
w6
d
w5
w7
b'
w3
a
w4
b
d'
w2
w1
c'

(f)

formation of a C(7) β--fused-γ-lactone is also relatively strain free. This is in agreement with the prediction of Hendrickson(35) and the cyclopentene and lactone rings are fused at his d-d' and b-c bonds respectively (Fig. 2.13).

The related compounds bromohelanin and the oxide of helanin (Table XXI) provide an example of the change in conformation of the cycloheptane in order to accommodate the requirements of the gross structure.

Although both these molecules have identical modes of fusion of the smaller rings, the latter compound has a cycloheptane ring which has adopted a conformation somewhere between the twist chair and chair, presumably in order to be able to form the oxygen bridge between the five and seven membered carbocycles.

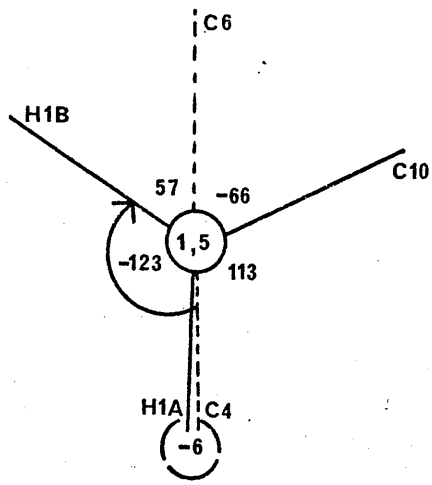
The conformation of the cycloheptane ring in mikanokryptin is much closer to a chair than a twist chair and Fig. 2.14 illustrates that relatively little additional strain is imposed on an isolated chair when it is fused to the smaller rings with the observed stereochemistry. Cycloheptene rings in guianolides generally adopt a twist chair conformation but again the minimum energy stereochemistry of the isolated ring may not always represent the most stable conformation in a crystal structure.

Further calculations are required to allow for the different locations of the C_2 axis or Cs plane in the non-symmetrical seven-membered rings before all the observed structures can be interpreted in terms of the stereochemistry of ring fusion.

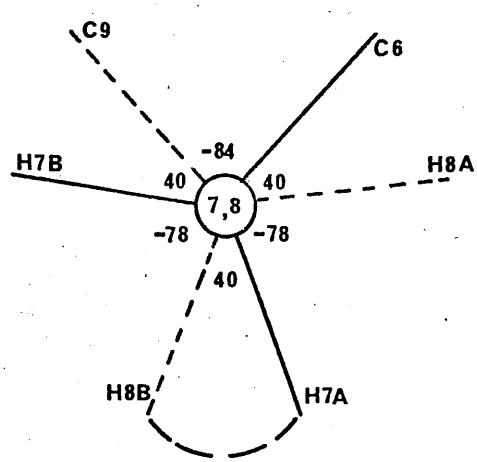
Fig. 2.14 Mikanokryptin: Stereochemistry in the vicinty of ring fusions.

(a) and (b) Newman projections down the C(1)-C(5) and C(7)-C(8) bonds respectively of calculated (FFI) 1-Methylidene-cycloheptane (chair conformation).

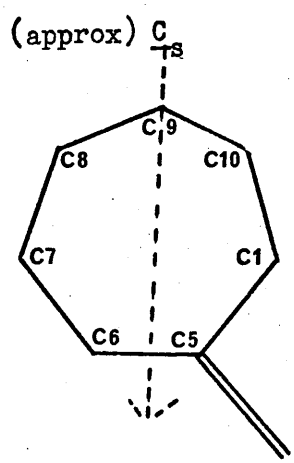
(c) Location of the approximate C_s plane in Mikanokryptin.


C6
H1B
C10
57
-66
1,5
-123
113
H1A
C4
-6

(a)


C9
C6
-84
H7B
40
40
H8A
7,8
-78
-78
40
H8B
H7A

(b)


(approx) C_s
C9
C8
C10
C7
C1
C6
C5

(c)

The mean of the valency angles in the cycloheptane ring is 115.4° and this is very similar to that found in other guianolides (40). This infers that the average Csp^3 valence angle is less distorted in the mikanokryptin structure since this mean includes the lone Csp^2 angle thus supporting previous statements regarding the stabilising effect of this atom.

The cyclopentenone ring is fused to the seven-membered carbocycle at C(1) and C(5) with the C(4)—C(5)—C(1)—C(2) torsion angle adopting a value of 4°. Inspection of a Dreiding model of the larger ring shows that its Cs chair form would allow complete eclipsing of the C(4) - C(5) and C(1) - C(2) bonds and that increasing pseudo-rotation towards the twist chair produces greater staggering. The torsion angles in the smaller carbocycle clearly indicate that it is almost planar and this is supported both by the maximum displacement (0.02A° for C(1)) from the mean plane through the atoms of this ring and by calculations using the algorithm of Cremer and Pople (28) which indicate a flattened envelope ($q = 0.03\ A^\circ, \Phi = 2^\circ$). A similar though less flattened envelope has also been observed in berlandin. The mean of the endocyclic valence angles is 108° in the mikanokryptin cyclopentenone ring and 107° in the corresponding portion of the berlandin structure. These values compare very favourably with the expected angle of 108° for a planar cyclopentane.

The α-methylene - γ - lactone is transfused at C(7) - C(8) and adopts a conformation which is between the half chair with the approximate C_2 axis through the centre

of the C(7) - C(8) bond and the envelope with C(8) out of the plane of the other four atoms. In the notation of Cremer and Pople q = 0.25A° and ϕ = 23° and this is confirmed by the fact that C(7) and C(8) are displaced, by 0.14 and 0.28A° respectively, to opposite sides of the plane through C(11), C(12) and O(16).

The positive Cotton effect at 257nm for acetylmikanokryptin (29) has been correlated with a C(7)β - C(8) trans-fused lactone by Stöcklin et al (3). As stated previously, the absolute configuration was not determined in this analysis and the torsion angles in Table XVIII should have their signs reversed to represent the stereochemistry predicted by the Cotton effect. Thus the C(13) - C(11) - C(12) - O(18) torsion angle becomes +6° which supports the predictions of Beecham (27) regarding the relationship between the sign of the Cotton effect and the chirality of this chromophore in lactones trans-fused to six and seven-membered rings.

Table XIIa Costunolide: Final structure factors

The table shows:

L^* $|F_o|$ $|F_c|$ Phase($^\circ$)

* Reflections sorted into groups with common H,K indices (shown in each group heading).

0,0,L

2	175	179	180
4	30	29	0
8	12	10	180

0,1,L

1	179	201	90
2	394	375	90
3	93	97	90
4	448	470	90
5	85	84	270
6	20	20	90
7	62	63	90
8	25	25	270

0,2,L

0	142	128	0
1	815	905	180
2	665	669	0
3	28	4	180
4	149	154	0
5	130	127	180
6	98	98	180
7	39	42	0
8	73	70	0

0,3,L

1	705	746	90
2	769	772	90
3	8	7	270
4	34	37	270
5	55	57	270
6	41	40	90
7	30	30	270
8	15	14	90

0,4,L

0	413	42	0
1	380	380	180
2	242	225	0
3	79	77	180
4	20	9	180
5	49	44	180
6	32	30	0
7	92	89	0
8	48	49	180

0,5,L

1	184	183	270
2	275	282	270
3	148	141	90
4	7	1	270
5	88	83	270
6	27	25	90
7	11	12	90
8	15	15	90

0,6,L

0	232	239	180
1	281	275	180
2	82	83	0
3	46	35	0
4	14	3	180
5	96	92	0
6	135	135	0
7	30	27	180
8	15	14	180
9	17	16	0

0,7,L

1	82	84	270
2	16	17	90
3	224	229	270
4	48	47	270
5	68	71	90
6	73	74	90
7	25	27	270

0,8,L

0	139	135	180
1	380	395	0
2	209	213	0
3	77	79	0
4	83	82	0
5	32	34	0
6	26	25	180
7	10	12	180
8	11	13	0

0,9,L

1	76	73	270
3	26	3	270
4	48	50	90
5	72	71	90
6	15	14	270
7	39	40	90
8	32	33	90

0,10,L

0	223	230	0
1	65	60	0
2	29	27	0
3	15	7	180
4	46	44	0
6	7	8	0
7	24	25	180
8	7	5	180

0,11,L

1	38	37	90
2	75	74	90
3	92	95	90
4	102	103	90
5	19	17	90
7	15	15	90

0,12,L

0	129	129	0
1	47	53	180
2	21	21	180
4	34	32	180
5	11	11	180
6	31	33	180
7	18	16	180

0,13,L

1	95	93	90
2	41	40	90
3	47	47	90
5	8	3	90

0,14,L

0	34	35	180
1	21	19	180
2	17	17	0
3	64	63	180
4	43	42	180
5	36	39	180
6	24	24	180

0,15,L

1	51	52	90
2	17	19	90
3	8	0	270
4	9	8	90
5	13	13	270

0,16,L

0	30	27	0
1	22	25	180
2	39	43	180
3	20	19	180
4	13	12	180

0,17,L

1	16	17	90
3	9	10	90

0,18,L

0	15	16	180
1	11	13	180
2	12	11	0

1,0,L

1	409	436	270
2	113	109	180
3	127	117	270
4	133	131	0
5	128	130	270
6	31	33	180
7	56	58	90

1,1,L

0	417	437	270
1	596	652	115
2	306	307	224
3	281	283	157
4	49	49	99
5	65	58	68
6	26	25	148
7	20	21	51
8	28	26	265

1,2,L

0	100	88	90
1	640	676	309
2	557	560	36

1,2,L

3	96	93	351
4	91	84	252
5	124	128	229
6	69	70	71
7	42	43	331
8	25	25	224

1,3,L

0	299	303	90
1	672	697	201
2	105	94	170
3	218	220	110
4	38	44	284
5	73	79	114
6	49	48	169
7	61	61	259
8	7	2	215

1,4,L

0	308	315	270
1	601	603	9
2	492	469	122
3	320	335	250
4	85	78	250
5	63	65	281
6	31	30	157
7	41	41	229
8	32	33	347

1,5,L

0	90	87	90
1	480	486	149
2	128	133	126
3	267	269	124
4	57	61	178
5	59	59	184
6	65	62	310
7	14	13	266
8	36	35	117

1,6,L

0	49	47	270
1	221	221	108
2	190	169	229
3	290	287	296
4	60	55	171
5	42	41	164
6	70	73	345
7	32	31	268
8	12	12	240
9	18	19	323

1,7,L

0	116	104	90
1	201	199	189
2	36	39	79
3	42	39	184
4	104	98	299
5	34	38	267
6	54	52	278
7	34	32	107
9	8	9	60

1,8,L

0	93	97	90
1	81	83	301
2	231	228	234
3	33	34	234
4	26	24	322
5	29	31	357
6	45	45	293
7	11	10	267
8	34	33	1

1,9,L

0	180	176	270
1	57	55	294
2	110	104	350
3	75	71	275
4	90	96	246
5	42	42	44
6	14	12	14
7	18	17	153
8	22	21	39

1,10,L

0	22	25	270
1	51	50	234
2	88	93	334
3	51	49	11
4	21	22	358
5	81	79	346
6	17	17	316
7	30	29	26

1,11,L

0	8	5	270
1	13	11	100
2	75	76	252
3	57	52	277
4	48	45	325
5	39	36	14
6	17	15	151
7	24	23	73

1,12,L

0	18	19	270
1	24	23	326
2	56	51	342
3	82	83	345
4	39	39	22
5	14	15	320
6	12	12	19
7	15	14	104

1,13,L

0	64	63	270
1	48	45	130
2	47	46	292
3	16	16	284
4	52	52	65
5	13	13	93
6	18	19	106

1,14,L

0	64	60	270
1	60	59	293
2	30	32	318
3	12	11	232
4	12	10	331
5	18	18	349
6	10	10	101

1,15,L

0	9	8	90
1	44	41	246
2	29	31	2
3	29	32	101
4	24	25	34
5	17	17	104

1,16,L

0	50	50	270
1	25	24	37
2	26	28	271
3	16	15	224
4	10	11	330
5	13	13	219

1,17,L

1	14	15	87
2	18	17	346
3	15	14	23
4	8	7	357

1,18,L

0	17	20	270
1	14	14	228
2	19	18	265

2,0,L

0	352	354	0
1	314	327	270
2	43	43	180
3	6	9	270
4	167	173	0
5	36	38	90
6	14	14	180
7	30	31	270
8	14	12	0

2,1,L

0	257	257	0
1	140	131	96
2	313	312	129
3	78	74	73
4	33	37	133
5	10	8	291
6	101	106	27
7	39	39	296
8	17	17	120

2,2,L

0	488	500	0
1	511	523	171
2	418	414	299
3	168	169	8
4	72	76	30

2,2,L

5	46	41	253
6	40	41	132
7	35	38	127
8	8	6	237

2,3,L

0	25	20	180
1	409	402	341
2	79	75	264
3	59	62	57
4	96	98	106
5	66	66	127
6	42	45	12
7	33	35	150
8	16	13	357

2,4,L

0	9	10	0
1	303	295	8
2	127	139	3
3	56	59	45
4	133	134	261
5	183	184	126
6	50	49	14
7	40	41	42
8	17	15	26

2,5,L

0	292	276	180
1	126	126	117
2	296	306	145
3	113	100	246
4	59	59	38
5	63	63	75
6	17	17	170
7	57	57	189
8	13	12	220
9	16	16	192

2,6,L

0	200	206	0
1	76	71	164
2	123	126	7
3	244	250	66
4	79	76	188
5	58	59	46
6	56	54	270
7	34	31	168
9	7	8	97

2,7,L

0	93	93	180
1	137	140	223
2	232	232	156
3	118	117	71
4	107	107	157
5	28	30	131
6	81	82	194
7	34	34	152

2,8,L

0	13	14	0
1	83	80	95
2	173	172	344
3	79	75	175
4	56	50	201
5	33	31	61
6	46	43	231
7	9	8	187
8	25	25	307

2,9,L

0	73	75	180
1	137	132	121
2	126	122	135
3	44	39	242
4	146	143	128
5	70	71	181
6	37	36	217
7	20	19	329
8	9	7	226

2,10,L

0	194	196	0
1	88	96	39
2	64	64	118
3	81	81	183
4	46	46	219
5	52	55	264
6	10	10	201
7	14	14	350
8	16	19	251

2,11,L

0	133	135	180
1	79	79	112
2	58	56	26
3	57	58	120
4	36	36	193
5	52	53	253
7	13	14	62

2,12,L

0	25	23	180
1	125	124	144
2	22	23	317
3	68	65	186
4	17	17	328
5	10	11	96
6	16	15	202
7	13	14	260

2,13,L

1	66	63	72
2	23	23	139
3	55	55	186
4	8	7	276
5	10	12	239
6	27	27	22

2,14,L

0	10	2	0
1	30	30	53
2	35	35	222
3	43	42	110
4	14	16	31
5	11	12	137
6	9	11	42

2,15,L

0	27	29	180
1	28	28	37
2	32	33	237
3	18	17	131
5	8	7	7

2,16,L

1	13	11	167
3	9	9	117
4	12	12	300

2,17,L

0	20	21	0
1	8	7	9
2	36	38	155
3	10	12	13

2,18,L

0	6	4	0
1	16	18	265

3,0,L

1	188	193	90
2	344	333	180
3	269	268	90
4	190	202	0
5	33	34	270
6	8	3	0
7	15	15	270
8	30	30	0

3,1,L

0	64	69	270
1	92	92	116
2	158	153	182
3	99	104	303
4	159	166	295
5	48	48	172
6	55	57	276
7	46	45	137
8	7	8	253

3,2,L

0	206	197	90
1	155	147	353
2	88	95	257
3	237	242	339
4	141	145	210
5	24	26	228
6	61	62	316
7	46	46	47
8	60	58	317

3,3,L

0	417	424	90
1	88	89	210
2	213	216	275

3,3,L

3	137	142	43
4	187	192	203
5	98	101	100
6	62	60	355
7	33	34	0
8	19	16	337

3,4,L

0	178	170	270
1	336	336	305
2	37	39	92
3	50	47	281
4	124	123	274
5	103	101	18
6	27	27	348
7	24	23	359
8	8	7	185
9	19	20	148

3,5,L

0	141	147	270
1	112	113	250
2	142	152	23
3	63	66	181
4	60	62	26
5	163	164	6
6	83	86	254
7	45	43	42
8	25	24	71
9	9	11	92

3,6,L

0	63	61	270
1	52	51	343
2	130	133	206
3	248	258	314
4	60	59	355
5	7	9	236
6	41	46	75
7	30	32	99

3,7,L

0	129	131	270
1	61	61	170
2	149	149	311
3	90	87	56
4	45	50	317
5	54	55	313
6	36	38	63
7	39	41	110
8	26	25	223

3,8,L

0	195	201	270
1	57	55	335
2	198	199	344
3	31	29	20
4	105	102	104
5	68	68	17
6	50	51	50
7	21	22	282
8	11	9	55

3,9,L

0	208	211	270
1	67	69	240
2	21	19	321
3	27	25	166
4	119	117	317
5	42	41	131
6	28	29	160
7	10	9	293
8	22	23	224

3,10,L

0	89	89	270
1	122	124	28
2	13	15	187
3	46	44	325
4	108	107	5
5	15	15	51
6	28	29	261
7	10	9	351

3,11,L

0	140	137	270
1	130	130	78
2	42	39	292
3	56	55	212
4	22	22	214
5	35	34	145
6	11	11	5
7	14	15	183

3,12,L

0	63	61	90
1	47	47	324
2	94	91	306
3	71	67	21
4	27	29	253
5	20	21	286
6	20	22	346
7	19	21	312

3,13,L

0	90	88	90
1	39	37	171
2	69	71	245
3	32	31	24
5	27	28	68

3,14,L

1	51	50	355
2	16	15	147
3	20	21	236
4	18	17	269
5	23	22	314
6	26	28	300

3,15,L

0	8	6	90
1	19	19	214
3	19	21	16
4	15	14	124
5	12	13	342

3,16,L

0	13	13	270
1	41	43	250
2	30	31	165
3	22	22	316

3,17,L

0	25	27	90
1	25	26	235
2	6	7	18
3	8	8	145

3,18,L

0	10	11	270
1	7	6	179

4,0,L

0	338	332	180
1	214	210	90
2	110	107	180
3	97	90	90
4	107	106	180
5	9	13	90
6	93	95	180
7	55	54	90
8	13	13	180

4,1,L

0	330	316	180
1	77	72	53
2	291	307	44
3	224	237	287
4	136	134	262
5	74	78	106
6	83	83	205
7	33	32	249
8	19	19	266

4,2,L

0	137	137	180
1	58	63	280
2	219	228	151
3	133	143	137
4	109	111	226
5	77	77	94
6	23	19	143
7	42	39	52
8	7	5	330
9	5	2	167

4,3,L

0	112	109	180
1	113	117	121
2	224	232	222
3	73	70	225
4	71	73	110
5	67	71	278
6	36	37	295
7	46	48	225
8	30	30	218

4,4,L

1	90	87	126
2	67	67	240
3	126	133	102
4	48	50	172
5	21	21	235
6	34	33	108
7	16	15	291
9	8	9	56

4,5,L

0	39	35	180
1	158	171	56
2	76	79	158
3	45	44	195
4	76	72	227
5	16	15	225
6	37	36	190
7	28	28	148
8	11	12	41

4,6,L

0	29	33	0
1	128	132	120
2	72	74	227
3	94	93	248
4	62	63	300
5	134	140	116
6	19	17	311
7	29	32	324
8	11	9	124

4,7,L

0	77	76	180
1	152	155	88

4,12,L

5	7	7	348
6	16	15	267

4,13,L

0	43	46	180
1	36	37	306
2	32	33	349
3	14	13	253
4	54	57	173
5	7	8	15
6	20	20	216

4,14,L

0	34	34	0
1	10	7	99
2	22	21	63
3	16	16	22
4	20	22	339
5	11	13	333

4,15,L

0	36	36	0
1	26	26	301
2	37	39	122
3	39	41	171
4	8	8	129
5	7	7	13

4,16,L

0	39	43	0
1	6	4	54
2	7	7	43
3	17	16	347
4	10	10	110

4,17,L

1	11	12	92
2	17	18	149

5,0,L

1	348	374	90
2	103	104	180
3	11	10	90
4	42	41	0
5	13	12	90
6	26	25	180
7	18	19	90

5,1,L

0	66	63	90
1	283	290	12
2	132	132	189
3	92	97	16
4	65	67	214
5	37	37	238
6	27	26	302
9	6	7	108

5,2,L

0	136	131	90
1	217	222	190
2	83	88	239
3	195	205	66
4	58	58	304
5	77	81	124
6	23	24	294
7	19	21	254

5,3,L

0	78	80	270
1	105	106	3
2	113	121	272
3	97	97	337
4	28	26	319
5	61	61	321
6	52	49	299
7	22	23	40
8	16	16	284

5,4,L

0	54	55	90
1	48	47	275
2	20	19	296

4,7,L

2	137	131	187
3	11	10	28
4	94	97	54
5	77	79	167
6	24	23	234
7	10	9	101
8	8	6	224

4,8,L

0	54	51	180
1	120	118	173
2	31	33	352
3	112	113	92
4	70	74	169
5	20	18	281
6	28	26	268
7	19	19	123
8	18	20	171

4,9,L

0	68	64	180
1	79	81	187
2	23	13	200
3	144	146	54
4	61	62	187
5	34	34	239
6	18	17	148
7	22	22	202
8	5	6	317

4,10,L

0	61	59	180
1	17	16	43
2	27	24	326
3	74	73	150
4	34	35	194
5	61	63	86
6	13	14	228
7	10	11	200

4,11,L

0	22	16	180
1	21	21	29
2	37	36	106
3	45	45	256
4	61	60	198
5	26	28	179
6	7	5	55
7	10	8	265

4,12,L

0	33	32	0
1	58	56	8
2	44	42	112
3	14	14	80
4	32	31	79

5,4,L

3	44	43	243
4	48	50	253
5	24	22	258
6	57	56	327
7	59	62	74

5,5,L

1	115	117	306
2	126	126	280
3	71	69	19
4	93	98	235
5	85	88	358
6	50	52	339
8	11	10	317

5,6,L

0	107	106	270
1	95	92	301
2	40	38	338
3	52	54	336
4	39	38	315
5	32	30	78
6	50	52	85
7	32	33	37
8	13	12	52

5,7,L

1	27	28	206
2	21	24	254
3	40	41	36
4	147	150	333
5	72	72	352
6	50	51	173
7	23	22	19
8	5	3	246

5,8,L

0	84	87	270
1	69	70	352
2	41	44	61
3	92	91	292
4	58	59	158
5	56	55	57
6	43	43	21
7	16	17	109

5,9,L

1	22	24	217
2	85	83	44
3	56	54	28
4	45	44	226
5	23	22	155
6	16	16	25
7	12	12	240

5,10,L

1	33	33	74
2	95	94	208
3	22	19	212
4	58	58	78
5	30	29	9
6	21	20	79
7	7	8	261

5,11,L

0	22	23	90
1	43	43	129
2	47	46	84
3	62	62	258
4	21	20	303
5	30	28	63
6	25	27	226
7	7	6	83

5,12,L

0	35	35	90
1	35	35	180
2	34	33	182
3	13	12	330
4	28	27	127
5	7	3	8
6	24	24	284

5,13,L

0	41	43	90
1	17	17	290
2	25	24	265
3	35	36	269
5	14	14	167
6	9	10	268

5,14,L

0	12	11	90
1	46	45	240
2	8	5	355
3	26	27	83
4	9	11	80
5	32	32	330

5,15,L

1	8	8	241
2	19	18	279
3	15	15	254
4	16	16	141

5,16,L

0	5	7	90
1	9	10	90
2	27	29	74
3	20	21	22

5,17,L

0	5	5	270
1	11	10	296

6,0,L

0	17	18	180
1	65	64	270
2	51	53	180
3	116	115	90
4	113	116	180
5	112	114	90
6	11	10	180
7	44	42	90
8	7	4	180

6,1,L

0	12	14	0
1	187	186	57
2	102	101	164
3	112	117	286
4	32	33	289
5	24	27	58
6	14	15	219
7	57	57	176
8	25	27	252

6,2,L

0	116	116	180
1	50	52	33
2	165	166	127
3	156	157	123
4	85	86	138
5	35	33	145
6	29	31	245
7	14	14	56
8	21	22	252

6,3,L

0	151	150	0
1	120	120	44
2	99	100	286
3	37	38	85
4	53	51	164
5	34	33	249
6	109	115	210
7	17	17	263
8	5	6	9

6,4,L

0	143	140	180
1	120	124	187
2	208	217	136
3	49	52	208
4	28	28	277
5	45	44	48
6	31	30	179
7	18	17	205
8	18	18	267

6,5,L

0	159	158	0
1	85	87	220
2	34	32	150
3	67	69	101
4	108	111	265
5	53	52	246
6	10	10	161
7	14	17	352
8	10	10	46

6,6,L

0	105	107	180
1	39	39	73
2	71	73	155
3	41	37	320
4	54	55	112
5	55	56	254
6	14	15	162
7	21	20	317
8	13	15	311

6,7,L

0	90	88	0

6,7,L

1	25	26	213
2	70	70	313
3	118	119	290
4	21	21	74
5	47	47	100
6	11	12	294
7	15	18	352

6,8,L

0	38	38	0
1	20	21	57
2	17	20	283
3	78	78	336
4	43	40	189
5	37	38	116
6	13	12	20
7	7	4	104

6,9,L

0	13	10	180
1	69	71	276
2	57	58	67
3	46	44	87
4	24	26	9
5	38	41	255
6	31	33	349
7	15	14	34

6,10,L

0	27	27	180
1	27	28	298
2	81	80	1
3	30	31	116
4	37	34	156
5	25	25	32
6	23	24	158
7	10	12	113

6,11,L

0	34	36	180
1	19	14	127
2	58	59	81
3	64	67	314
4	21	19	202
5	34	33	40
6	6	6	238

6,12,L

0	76	76	0
1	50	50	299
2	46	45	214
3	38	38	164
4	8	6	179
5	21	22	69

6,13,L

0	15	8	180
1	33	36	7
2	34	34	266
3	13	15	308
4	31	32	114
5	25	26	264

6,14,L

0	13	12	180
1	40	44	236
2	23	21	120
3	11	10	256
4	9	9	62

6,15,L

1	28	28	330
2	7	7	3
3	16	16	311

6,16,L

0	13	14	180
1	14	15	266
2	15	15	137

7,0,L

1	22	26	270
2	34	35	180
3	31	28	270
4	18	18	180
5	78	81	90
6	8	4	0
7	14	17	90

7,1,L

0	122	127	90
1	124	126	321
2	90	91	289
3	41	40	23
4	56	60	32
5	85	86	4
6	39	41	212
7	25	24	349
8	11	13	146

7,2,L

0	87	91	90
1	54	58	229
2	25	26	167
3	60	59	230
4	64	62	93
5	15	17	86
6	26	25	69
7	25	27	86
8	13	13	107

7,3,L

0	51	51	270
1	104	107	266
2	42	46	80
3	102	101	19
4	29	29	257
5	59	61	274
6	37	35	231
7	11	12	90
8	15	16	156

7,4,L

0	107	110	270
1	92	97	168
2	66	65	143
3	64	63	87
4	90	91	96
5	14	13	243
6	17	17	134
7	7	7	173
8	16	19	17

7,5,L

0	52	51	90
1	13	11	323
2	29	28	44
3	35	34	221
4	77	76	302
5	37	37	276
6	29	29	109
7	17	18	136

7,6,L

1	63	62	168
2	14	13	119
3	30	31	136
4	39	39	179
5	20	20	319
6	19	19	37
7	14	15	21

7,7,L

0	17	17	270
1	88	87	316
2	71	72	92
3	55	53	293
4	22	23	254
5	46	49	152
6	17	16	227
7	14	15	269

7,8,L

0	25	24	90
1	51	52	136
2	53	55	172
3	34	35	91
4	29	26	288
5	25	24	112
6	13	12	138
7	16	19	305

7,9,L

0	37	37	90
1	65	68	60
2	31	31	104
3	62	60	307
4	31	31	168
6	6	7	11

7,10,L

0	90	88	90
1	29	33	132
2	47	50	75
3	17	15	161
4	52	53	184
5	15	13	30

7,10,L

6	17	17	299

7,11,L

0	76	78	90
1	35	33	314
2	37	34	171
3	9	6	74
4	32	33	167
5	23	23	19
6	10	12	23

7,12,L

0	66	72	90
1	19	18	267
2	47	45	154
3	16	19	205
4	22	23	70
5	7	8	86

7,13,L

1	31	33	141
2	28	29	125
3	10	10	257
4	14	14	114

7,14,L

0	10	11	90
1	22	23	240
2	22	24	118
3	9	9	311
4	19	20	139

7,15,L

0	34	37	90
1	11	11	224
2	6	8	352

7,16,L

0	17	17	270

8,0,L

0	56	59	0
1	24	26	90
2	76	79	0
3	60	63	270
4	48	46	180
5	21	23	270
6	8	9	180
7	31	30	270

8,1,L

0	85	83	0
1	85	87	57
2	46	44	102
3	75	76	192
4	51	50	41
5	50	50	11
6	12	10	146
7	18	18	285

8,2,L

0	62	65	0
1	58	56	223
2	73	75	265
3	53	52	201
4	29	29	147
5	17	16	299
6	17	18	108
7	13	11	158

8,3,L

0	70	70	0
1	29	30	13
2	65	68	220
3	58	60	60
4	98	97	17
5	43	40	254
6	31	32	307
7	13	12	37

8,4,L

0	129	127	180
1	28	25	299
2	42	41	194
3	45	46	179
4	11	8	158
6	13	13	128
7	15	14	69

8,5,L

0	52	53	0
1	36	37	233
2	11	9	135
3	118	121	346
4	84	86	304
5	13	15	230
7	12	10	252

8,6,L

0	48	48	180
1	106	106	277
2	63	62	177
3	39	40	40
4	15	16	337
5	44	44	59
6	16	16	118
7	14	16	67

8,7,L

0	31	32	180
1	93	96	264
2	71	72	334
3	85	85	338
4	37	35	221
5	8	8	318

8,8,L

0	21	20	180
1	85	88	279
2	39	42	85
3	51	53	353
4	20	21	70
5	18	19	69
6	9	9	76

8,9,L

0	58	56	0
1	79	78	322
2	41	41	2
3	49	52	319
4	34	36	159
5	12	14	3

8,10,L

0	38	36	0
1	48	47	311
2	27	28	84
3	43	43	302
4	16	18	110
5	7	6	74

8,11,L

0	35	37	0
1	16	17	317
2	32	34	29
3	7	6	250
4	9	7	273
5	8	8	4

8,12,L

0	15	13	180
1	17	18	215
2	21	24	67
3	9	11	227
4	14	14	111

8,13,L

0	10	13	0
2	12	11	320
3	8	11	247

8,14,L

2	21	20	204

8,15,L

0	4	4	0

9,0,L

1	65	66	90
2	44	45	0
3	36	33	90
4	23	25	180
5	11	8	270
6	22	24	0
7	8	9	270

9,1,L

0	90	94	90
1	138	139	289
2	110	110	216
3	55	53	116
4	32	31	84
5	25	25	139

9,1,L

6	10	9	195
7	16	17	230

9,2,L

0	92	96	90
1	82	82	22
2	49	50	156
3	31	30	152
4	9	6	301
5	17	18	47
6	27	28	233
7	14	15	247

9,3,L

0	37	36	90
1	14	14	203
2	100	100	124
3	61	61	97
4	40	42	170
5	16	16	230
6	11	11	331
7	17	21	51

9,4,L

0	110	114	90
1	42	40	260
2	50	50	130
3	36	36	306
4	42	44	198
5	20	20	209
6	21	22	244

9,5,L

0	115	118	90
1	36	37	211
2	108	104	118
3	11	10	98
4	29	31	221
5	26	27	332
6	17	18	95

9,6,L

0	53	50	90
1	44	40	180
2	85	84	178
3	41	43	211
4	24	25	165
5	16	16	262
6	15	16	165

9,7,L

0	7	2	90
1	39	41	194
2	73	76	88
3	47	45	304
4	10	8	335
5	16	15	29
6	13	12	283

9,8,L

0	7	6	90
1	82	81	215
2	25	26	158
3	11	12	99
4	25	26	138
5	17	16	173

9,9,L

0	34	34	90
1	35	34	47
2	15	17	346
3	43	46	273
5	10	8	267

9,10,L

0	29	30	270
1	18	19	141
2	27	29	67
3	16	14	98
4	16	17	154
5	13	12	73

9,11,L

0	24	22	90
1	19	21	341
2	21	20	298
3	5	3	357
4	6	7	113

9,12,L

0	12	13	90
1	18	18	72
2	12	13	84
3	12	13	120

9,13,L

0	5	5	90
1	16	16	329
2	17	16	103

10,0,L

0	72	63	0
1	106	95	270
2	18	17	180
3	49	45	270
6	10	8	0

10,1,L

0	11	3	0
1	75	72	326
2	21	21	17
3	35	36	20
4	12	11	32
5	24	26	351
6	9	9	185

10,2,L

0	65	63	180
1	69	69	252
2	45	43	15
3	25	25	275
4	21	24	66
5	13	15	36

10,3,L

0	112	109	0
1	31	31	335
2	15	12	145
3	38	39	314
4	18	18	342
5	10	11	351
6	11	12	133

10,4,L

0	46	44	0
1	78	77	327
2	22	22	52
3	15	14	68
4	12	15	103
5	8	9	261
6	16	16	344

10,5,L

0	29	30	0
1	42	43	218
2	23	25	273
3	29	29	347
4	12	10	103
5	8	8	197

10,6,L

0	21	22	0
2	16	15	135
3	20	20	281
4	17	19	0
5	19	19	5

10,7,L

0	24	25	180
1	8	8	221
2	21	21	60
3	12	13	337
4	14	13	196
5	7	10	87

10,8,L

0	7	8	180
1	30	29	287
2	9	6	180
3	6	4	311
4	17	18	317
5	11	12	290

10,9,L

0	23	24	180
1	10	7	302
2	18	19	305
3	5	5	118

10,10,L

0	8	11	0
1	24	24	211
2	24	24	183
3	23	24	280

10,11,L

0	15	15	0
1	12	13	345
2	8	9	287
3	9	7	351

10,12,L

0	25	25	180
1	13	14	212

11,0,L

1	45	43	90
2	23	26	180
3	7	0	90
4	13	14	180
5	8	10	270

11,1,L

0	55	58	90
1	18	17	179
2	18	16	122
3	29	30	134
4	10	8	131
5	13	12	201

11,2,L

0	20	20	90
1	7	9	235
2	13	13	235
3	18	17	4
4	18	18	233

11,3,L

0	17	18	90
1	12	11	210
2	42	44	107
4	11	9	102

11,4,L

0	12	6	90
1	20	18	24
2	30	31	187
3	24	25	240
4	18	17	207
5	6	4	126

11,5,L

0	35	34	90
1	7	5	57
2	17	19	47
3	7	7	134
4	6	6	130

11,6,L

0	20	22	90
1	11	12	226
2	14	14	267
3	5	1	214
4	22	22	115

11,7,L

0	18	19	90
1	6	6	318
2	16	16	85
4	15	15	327

11,8,L

0	6	5	270
1	6	7	267
2	10	7	186
3	29	28	93

11,9,L

0	9	9	270
1	16	16	60
2	9	9	37
3	12	12	191

11,10,L

0	19	18	270
1	6	5	209
2	15	14	118

12,0,L

0	15	17	0
1	17	18	270
2	21	21	180
3	10	10	270
4	10	10	0

12,1,L

0	11	10	180
2	10	9	289
3	22	21	11
4	7	8	100

12,2,L

0	23	25	180
1	25	27	241
2	26	26	16
3	10	10	25
4	9	7	44

12,3,L

0	14	13	180
1	14	14	343
2	6	5	332
3	8	8	233
4	13	10	241

12,4,L

0	9	10	180
1	27	28	341
2	10	11	34
3	16	16	230

12,5,L

2	17	16	229
3	12	10	115

12,6,L

0	20	20	0
2	18	16	271
3	9	8	293

12,7,L

0	13	13	180
1	7	7	0

12,8,L

1	10	11	342

13,0,L

1	8	7	90
2	38	30	180

13,1,L

0	9	10	90
1	16	13	36
2	22	17	104

13,2,L

0	12	10	90
1	19	17	153

13,3,L

0	11	11	90

13,4,L

0	7	7	270
1	8	7	111

Table XXII Mikanokryptin: Final structure factors

The table shows:

L^* $|F_o|$ $|F_c|$ Phase(°)

* Reflections sorted into groups with common H,K indices (shown in each group heading).

0,0,L

18	59	56	180
16	40	43	180
14	85	85	0
12	237	243	180
10	67	68	0
8	86	88	0
6	194	188	0
4	316	306	0
2	99	89	180

0,-1,L

18	81	85	90
17	23	23	90
14	132	132	90
13	129	134	270
12	175	185	90
11	43	49	270
10	52	49	270
9	134	133	90
8	141	147	90
7	285	273	90
6	199	190	90
5	130	121	270
4	302	278	90
3	475	459	270
2	101	98	90

0,-2,L

18	51	51	180
17	34	29	180
16	33	36	180
15	67	66	180
13	134	137	0
12	48	48	0
11	67	66	180
10	92	89	0
8	119	117	180
7	131	128	0
6	545	500	0
5	230	206	0
4	246	233	0
3	667	631	0
2	30	27	0
1	1034	1086	180
0	567	567	0

0,-3,L

18	58	57	90
16	28	32	270
15	63	65	270
14	138	142	90
13	51	56	270
12	59	55	90
11	68	67	270
10	283	295	270
9	50	42	270
8	14	15	270
7	230	228	270
6	90	73	90
5	301	281	90
4	199	185	90
3	347	306	90
2	282	259	270
1	100	102	90

0,-4,L

18	38	39	0
17	19	9	180
16	51	51	0
14	28	27	0
12	89	90	0
11	53	54	180
10	76	77	0
9	24	25	180
8	45	42	180
7	191	186	180
6	98	96	0
5	201	195	0
4	170	154	180
3	19	17	0
2	60	62	0
1	139	141	0

0,-5,L

17	35	33	90
16	63	56	270
15	102	102	270
14	30	29	90
13	41	37	270
12	39	36	90
11	43	37	90
10	162	173	270
9	141	146	270
8	259	259	90
7	63	59	90
6	168	170	270
5	57	59	90
4	48	58	90
3	426	416	90
1	149	143	270

0,-6,L

17	20	11	180
16	83	81	0
14	56	53	0
11	25	29	180
10	89	85	0
9	13	16	0
8	82	87	0
7	23	15	180
6	19	18	180
5	144	138	0
4	76	73	180
3	18	15	0
2	165	163	180
1	26	22	180
0	465	465	0

0,-7,L

17	55	50	90
16	24	17	90
15	45	45	270
14	22	22	90
13	29	28	270
11	28	26	90
10	42	38	90
9	26	24	270
8	39	41	90
7	239	251	90
6	116	113	90
5	110	106	270
4	135	134	270
3	27	27	270
2	164	168	90
1	56	62	270

0,-8,L

15	61	57	0
13	78	73	0
12	34	34	0
11	36	33	180
10	70	72	0
9	22	22	180
8	43	47	0
6	124	124	0
5	58	59	0
4	148	144	0
3	85	88	0
2	86	86	180
1	124	122	180
0	48	54	180

0,-9,L

15	16	16	90
14	18	18	90
13	74	73	90
12	79	75	90
10	28	28	90
9	53	49	270
8	48	41	90
7	107	102	270
6	163	165	90
5	90	89	90
3	57	55	270
2	24	28	90
1	53	54	270

0,-10,L

14	16	14	180
13	33	35	0
11	41	39	180
10	20	17	180
9	25	28	0
8	23	25	0
6	45	42	0
5	15	7	180
4	22	24	180
3	52	49	0
2	84	86	0
1	41	41	180
0	104	104	0

0,-11,L

12	48	45	90
11	46	45	90
9	17	25	90
8	74	70	90
5	26	27	90
3	52	53	270
2	28	25	270
1	69	71	270

0,-12,L

10	38	39	180
9	23	25	180

0,-12,L

8	35	34	0
7	25	22	180
6	58	52	0
3	46	46	180
2	20	19	0
0	26	23	180

0,-13,L

5	20	14	90
4	27	28	270
3	32	32	90
2	17	19	270

-1,0,L

19	59	67	90
18	30	23	0
14	42	41	0
13	169	172	90
12	126	129	180
11	222	225	90
10	102	102	0
9	262	266	270
8	12	22	0
7	72	69	90
6	387	356	180
5	31	27	270
4	251	240	0
2	31	33	180
1	99	106	270

-1,-1,L

19	45	46	179
18	22	15	212
17	57	58	163
14	111	110	313
13	53	55	188
12	173	180	125
11	92	90	46
10	113	113	306
9	161	162	144
8	174	172	236
7	135	130	2
6	174	164	343
5	259	240	293
4	444	417	221
3	194	181	90
2	448	426	180
1	893	915	354
0	200	197	270

-1,-2,L

18	31	28	55
17	49	47	123
16	29	29	269
15	25	29	113
14	113	113	298
13	143	149	64
12	114	121	295
11	194	196	240
10	93	92	74
9	90	88	261
8	227	223	312
7	224	218	73
6	197	189	144
5	303	274	101
4	462	440	48
3	166	158	49
2	745	709	148
1	444	428	341
0	242	236	270

-1,-3,L

19	35	31	141
17	17	20	81
16	60	54	171
15	36	36	67
14	55	53	246
13	53	51	324
12	73	76	91
11	127	128	153
10	144	137	266
9	100	102	306
8	124	121	214
7	53	51	300
6	66	61	78
5	211	193	46
4	659	628	308
3	404	370	182
2	141	137	304
1	493	469	10
0	587	586	270

-1,-4,L

19	26	19	78
18	35	35	301
17	24	20	297
15	51	50	170
14	98	99	298
13	37	36	116
12	85	84	26
11	94	98	281
10	114	123	301
9	53	57	192
8	122	127	23
7	131	126	323
6	89	89	39
5	110	111	196
4	305	299	13
3	268	246	332
2	296	278	134
1	226	213	97
0	179	167	270

-1,-5,L

18	31	31	113
17	74	75	18
16	33	30	149
15	41	42	6
14	36	36	267
13	44	41	311
12	62	59	30
11	126	125	359
10	118	111	188
9	146	150	290
8	140	143	254
7	53	51	257
6	163	160	287
5	143	138	147
4	277	277	329
3	185	176	222
2	171	168	242
1	105	100	165
0	77	80	270

-1,-6,L

17	54	53	278
16	30	32	313
15	17	12	170
14	63	63	272
13	65	64	10
12	35	34	288
11	50	51	70
10	86	84	333
9	106	110	245
8	57	58	36
7	89	85	125
6	38	36	340
5	105	104	223
4	216	214	48
3	99	95	313
2	62	65	297
1	97	93	92
0	51	48	90

-1,-7,L

17	35	31	33
16	39	37	358
15	36	32	15
14	109	106	313
13	35	35	258
12	14	22	152
11	51	51	11
10	38	38	218
8	99	105	301
7	54	56	307
6	41	42	30
5	105	108	298
4	18	16	76
3	34	31	119
2	103	104	206
1	53	52	137
0	65	64	270

-1,-8,L

14	24	20	110
13	28	28	45
12	45	43	45
11	46	48	269
10	22	26	65
8	68	62	271
7	203	201	82
6	68	68	83
5	80	80	135
4	53	54	326
3	69	67	43
2	104	104	220
1	23	24	249
0	152	151	270

-1,-9,L

15	31	33	110
14	50	45	321
13	27	30	258
12	25	24	265
11	15	17	67
10	42	39	302

-1,-9,L

8	26	27	274
7	87	91	8
6	39	41	108
5	47	46	104
4	120	126	344
3	48	48	98
2	90	87	352
1	49	51	63
0	25	25	90

-1,-10,L

13	29	25	87
12	59	56	89
11	78	74	72
9	66	66	65
8	23	22	235
7	16	17	249
6	47	47	43
4	43	45	305
3	65	65	329
2	50	46	306
1	57	57	112
0	74	76	270

-1,-11,L

11	27	26	140
10	28	30	182
9	25	25	89
8	47	47	211
7	48	48	4
6	26	25	338
5	16	13	92
4	57	54	207
2	77	77	209

-1,-12,L

7	38	36	132
5	32	33	82
4	37	35	85
3	32	33	271
2	23	20	317
1	18	14	184

-1,-13,L

7	24	17	319
5	42	35	350
2	49	47	235
0	28	24	270

-1,-14,L

1	15	17	200

-2,0,L

19	24	28	270
18	31	25	180
17	45	41	270
15	22	17	90
14	56	56	180
13	82	85	90
12	125	133	180
11	94	99	90
10	102	99	180
9	273	273	270
8	78	77	0
7	67	53	90
6	287	273	180
5	108	103	270
4	370	344	180
3	444	431	270
2	57	59	180
1	465	443	90
0	1013	1061	0

-2,-1,L

19	19	14	307
18	33	29	240
16	40	38	3
15	35	34	308
14	87	88	186
13	110	111	306
12	126	133	3
11	138	143	180
10	129	135	196
9	187	188	56
8	272	266	262
7	205	196	170
6	298	285	130
4	107	111	240
3	182	179	213
2	631	612	5
1	745	725	163
0	63	66	0

-2,-2,L

18	62	63	156
17	23	28	115
16	20	19	225
15	86	87	243
14	54	56	94
13	40	47	112
12	59	62	47
11	113	119	138
10	117	117	186
9	127	125	202
8	130	124	242
7	100	105	266
6	142	136	105
5	79	76	130
4	326	306	169
3	477	464	301
2	494	471	280
1	427	413	206
0	559	540	180

-2,-3,L

18	33	31	257
17	53	49	232
16	63	59	154
15	91	92	335
14	38	38	129
13	115	117	211
12	68	72	339
11	204	211	344
10	163	168	214
9	146	144	359
8	122	126	292
7	127	126	264
6	50	39	64
5	381	361	89
4	140	135	296
3	310	283	105
2	279	269	323
1	215	207	37
0	13	7	0

-2,-4,L

18	44	39	99
17	56	54	95
16	84	86	64
15	72	68	256
14	57	59	253
13	29	26	83
12	15	19	296
11	117	120	81
10	92	88	225
9	235	229	238
8	112	109	269
7	177	178	232
6	211	212	251
5	165	155	294
4	293	288	163
3	164	161	218
2	278	263	61
1	273	258	288
0	376	353	180

-2,-5,L

18	26	30	266
17	17	14	332
16	59	55	220
15	23	25	322
14	67	67	338
13	45	45	306
12	60	59	209
11	73	77	1
10	69	67	257
9	53	57	252
8	22	23	265
7	82	82	0
6	12	12	233
5	299	303	6
4	110	111	151
3	116	112	59
2	20	23	55
1	255	255	203
0	113	118	0

-2,-6,L

16	78	79	41
15	28	27	7
14	42	43	241
13	36	34	276
12	36	38	234
11	20	16	50
10	41	39	78
9	93	96	266
8	178	180	278
7	112	120	329
6	150	147	154
5	162	159	2
4	213	209	225
3	105	105	274
2	131	131	156
1	99	94	22
0	36	35	180

-2,-7,L

17	35	31	113
15	23	16	165
14	16	13	215
13	35	31	326
12	85	83	310
11	39	40	53
10	22	22	334
9	54	56	29
8	97	99	238
7	31	38	106
6	142	144	163
5	175	176	338
4	133	133	278
3	85	86	252
2	142	146	356
1	124	130	226
0	63	68	180

-2,-8,L

16	27	29	75
15	49	46	324
14	28	27	29
13	97	93	289
12	24	25	317
11	26	25	303
9	62	61	109
8	27	24	193
7	89	93	295
5	155	158	85
4	40	45	95
3	95	94	298
2	122	125	164
1	23	20	124
0	157	155	180

-2,-9,L

15	15	18	19
14	21	19	184
13	46	47	130
12	62	61	0
11	34	28	345
10	20	15	67
9	36	34	255
8	36	36	332
7	70	65	270
6	50	50	122
5	96	95	78
4	74	74	351
3	41	38	341
2	25	21	337
1	50	51	296
0	126	130	180

-2,-10,L

13	24	23	332
12	50	47	203
11	23	22	180
10	36	32	115
9	57	58	253
8	64	65	77
7	37	39	259
6	46	44	279
5	44	44	117
4	100	102	119
2	81	77	58
1	24	27	140
0	37	39	0

-2,-11,L

12	21	22	58
11	24	20	32
10	24	27	44
9	39	44	157
8	31	30	92
7	19	18	22
6	18	20	142
5	33	30	15
4	45	41	116
2	30	32	339
1	46	45	338
0	21	22	180

-2,-12,L

10	39	39	123
9	27	28	191
7	34	35	96
6	23	22	357
5	16	13	5
4	17	7	71
3	61	61	244
2	20	12	5
1	24	24	254
0	24	21	180

-2,-13,L

6	15	12	197
4	28	23	300
3	35	35	118
2	46	44	215
1	28	31	354
0	20	19	180

-2,-14,L

1	17	20	247

-3,0,L

19	31	32	270
18	41	38	180
16	19	19	0
13	81	87	270
12	189	196	180
11	50	48	90
10	130	123	0
9	92	90	270
8	151	150	180
7	243	255	270
6	134	135	180
5	203	194	270
4	253	239	180
3	303	273	90
2	156	148	0
1	52	49	270

-3,-1,L

19	25	27	120
18	21	12	272
17	23	24	158
16	19	21	318
15	14	13	330
14	26	26	53
13	27	26	226
12	162	170	103
11	118	126	159
10	199	207	156
9	55	57	22
8	177	170	216
7	136	135	272
6	48	45	36
5	540	510	228
4	174	162	136
3	309	294	133
2	468	437	211
1	376	363	224
0	608	598	90

-3,-2,L

19	52	52	295
18	55	53	217
17	50	47	213
16	23	23	223
15	15	9	71
14	20	24	329
13	102	105	341
12	89	95	264
11	110	116	193
10	38	41	190
9	54	56	238
8	27	19	157
7	72	65	181
6	143	138	135
5	269	256	107
4	160	158	182
3	243	219	228
2	687	649	148
1	317	300	287
0	532	531	90

-3,-3,L

19	47	49	105
18	23	19	116
17	22	22	130
16	40	41	236
15	37	36	78
14	52	51	145
13	56	55	282
12	81	84	110
11	62	54	191
10	61	65	164
9	171	182	250
8	154	147	207
7	251	251	222
6	174	173	109
5	197	187	154
4	150	146	193
3	260	234	338
2	182	176	75
1	86	89	179
0	73	63	270

-3,-4,L

18	30	30	221
17	24	24	238
16	46	47	235
15	37	42	175
14	26	23	224

-3,-4,L

13	29	29	204
11	30	32	299
10	49	46	95
9	98	96	204
8	60	64	184
7	111	110	291
6	122	124	14
5	168	169	151
4	265	251	83
3	121	115	326
2	272	268	216
1	145	146	302
0	244	232	270

-3,-5,L

18	45	46	100
17	62	58	94
16	30	27	333
15	18	19	26
14	25	22	158
13	24	23	165
12	28	29	345
11	66	69	197
10	117	124	77
9	143	151	316
8	61	64	263
7	95	92	271
6	83	84	282
5	144	144	143
4	182	178	113
3	177	179	206
2	163	162	341
1	195	200	161
0	245	256	90

-3,-6,L

17	34	31	191
15	32	30	204
14	34	33	131
13	74	73	310
12	20	16	238
11	61	60	309
10	74	72	8
9	56	57	214
8	79	77	224
7	160	166	229
6	146	149	322
5	105	110	286
4	104	106	341
3	120	119	31
2	59	60	297
1	83	86	309
0	49	46	90

-3,-7,L

16	25	26	15
15	63	60	16
14	82	80	297
12	38	38	16
11	57	54	173
10	50	53	141
9	60	61	103
8	79	84	290
7	107	103	204
6	129	131	10
5	122	121	232
4	162	168	87
3	136	140	120
2	49	47	187
1	70	73	158
0	35	31	90

-3,-8,L

15	15	17	239
14	45	39	90
13	15	15	289
12	19	18	326
11	67	66	286
10	23	23	40
9	21	14	282
8	17	18	172
7	27	31	234
6	71	73	4
5	56	53	155
4	49	49	318
3	85	89	328
2	97	103	215
1	119	124	271
0	68	73	270

-3,-9,L

14	17	14	286
13	44	45	244
12	33	29	300
10	21	23	329
9	33	30	72
7	57	62	163
6	67	72	74
5	42	47	108
4	34	30	92
3	94	98	100
2	49	52	24
1	71	76	120
0	42	39	90

-3,-10,L

13	28	25	76
12	29	29	171
11	44	42	350
10	16	11	155
9	38	38	28
8	50	49	177
7	67	67	225
6	50	50	356
5	22	20	175
4	43	47	77
3	43	49	37
2	66	65	10
1	58	60	215
0	48	48	270

-3,-11,L

11	31	28	151
10	33	36	155
9	49	52	50
8	19	19	142
6	31	26	102
5	26	28	355
4	22	27	154
3	24	25	144
2	27	24	213
1	35	37	70
0	57	58	90

-3,-12,L

9	28	30	86
8	18	17	197
7	45	42	157
6	32	30	221
5	21	24	47
4	25	24	145
3	27	23	109
2	50	48	74
1	47	43	207
0	17	18	90

-3,-13,L

6	32	30	96
4	28	24	63
3	19	20	71
2	40	40	246

-4,0,L

19	20	22	90
18	30	31	0
17	61	59	270
15	49	45	90
14	81	87	180
13	83	83	90
12	20	16	180
11	137	139	90
10	40	39	0
9	25	23	270
8	190	194	0
7	57	47	270
6	119	114	180
5	168	164	90
4	80	79	0
3	208	196	90
2	438	414	0
1	112	115	90
0	648	631	180

-4,-1,L

18	39	40	258
17	20	24	157
16	47	46	9
15	46	47	214
14	49	50	185
13	62	65	16
12	83	88	1
11	177	188	169
10	171	183	148
9	94	95	66
8	66	71	13
7	135	140	246
6	133	137	130
5	184	185	183
4	354	361	124
3	201	192	169
2	59	60	329
1	347	326	180
0	43	39	180

-4,-2,L

17	30	27	311
16	36	31	235
15	39	43	359
14	103	105	6
13	133	136	144
12	69	68	263
11	98	103	113
10	116	115	262
9	139	139	130
8	154	162	316
7	38	41	148
6	175	171	230
5	141	135	142
4	136	130	25
3	204	194	134
2	258	242	273
1	442	419	32
0	100	98	180

-4,-3,L

18	35	38	271
17	88	89	211
16	63	62	107
15	17	18	175
14	23	23	308
13	93	91	172
12	79	78	355
11	51	50	345
10	91	100	134
9	161	169	194
8	97	96	115
7	45	47	75
6	150	151	249
5	123	120	152
4	109	100	222
3	161	156	153
2	233	226	256
1	32	35	12
0	21	15	0

-4,-4,L

18	55	55	88
17	24	24	92
15	63	59	227
14	64	64	342
13	52	50	39
12	87	86	161
11	111	114	60
10	54	50	291
9	82	83	201
8	141	144	303
7	97	95	144
6	199	195	254
5	205	202	183
4	53	49	63
3	401	406	114
2	17	17	117
1	73	80	127
0	67	71	0

-4,-5,L

17	43	43	223
16	63	61	186
15	62	62	120
14	56	59	321
13	25	27	37
12	52	55	214
11	45	48	206
10	63	60	18
9	80	83	156
8	184	194	228
7	40	42	3
6	32	32	23
5	45	44	355
4	145	145	73
3	143	150	226
2	25	25	25
1	169	170	166
0	180	190	0

-4,-6,L

16	56	53	88
15	29	32	340
13	15	19	262
12	33	38	183
11	62	61	127
10	40	40	64
9	25	21	191
8	45	48	299
7	111	112	349
6	119	121	117
5	97	93	33
4	45	38	337
3	200	202	96
2	122	124	85
1	50	53	14
0	93	98	180

-4,-7,L

16	31	30	174
15	56	58	148
14	39	37	141
13	57	58	17
11	49	50	148
10	60	57	292
9	100	105	53
8	42	44	206
7	118	122	268
6	97	100	241
5	111	111	352
4	68	70	19
3	65	72	311
2	204	217	291
1	70	63	196
0	105	113	0

-4,-8,L

15	16	5	174
14	64	62	15
13	24	22	266
11	58	55	2
10	28	27	122
9	61	56	65
8	60	61	111
7	38	36	325
6	43	44	230
5	60	61	114
4	54	55	60
3	24	22	119
2	92	96	94
1	56	61	11
0	24	24	0

-4,-9,L

14	23	29	144
13	23	19	20
12	68	66	349
11	30	28	198
9	31	33	244
8	34	36	121
6	97	101	232
5	15	19	51
4	78	80	50
3	90	90	41
2	37	37	270
1	57	60	228
0	106	108	180

-4,-10,L

13	20	14	11
12	60	60	187
11	24	28	357
10	21	22	21
9	24	25	254
8	32	37	62
7	51	51	73
6	58	59	270
5	22	25	56
4	39	40	61
3	88	87	106
2	65	66	68
1	26	21	64
0	85	87	0

-4,-11,L

11	41	42	202
10	22	22	41
9	43	40	165
8	18	18	167
7	17	12	145
6	20	19	163
5	45	44	225
4	71	68	109
3	27	29	110
2	34	30	61
1	24	27	76
0	67	67	180

-4,-12,L

8	15	11	159
7	74	71	69
6	26	19	123
5	31	30	13
4	39	37	342
3	22	27	64
2	31	34	109
0	26	25	0

-4,-13,L

5	20	15	159
3	30	28	80
2	38	34	237
1	33	26	27
0	20	24	180

-5,0,L

17	15	8	90
16	45	47	180
15	44	47	90
13	18	7	90
12	47	50	0
11	100	108	90
10	69	78	180
9	269	285	90
8	21	24	0
7	53	56	90
6	100	102	0
5	93	93	90
4	251	244	180
3	251	244	90
2	57	58	180
1	229	207	90

-5,-1,L

18	55	53	283
17	30	26	342
16	47	46	337
14	28	24	67
13	16	14	326
12	36	34	52
11	14	23	249
10	137	150	164
9	222	226	327
8	65	68	41
7	199	200	330
6	73	75	235
5	76	75	319
4	46	48	91
3	294	293	16
2	157	145	176
1	172	164	284
0	53	53	90

-5,-2,L

17	35	36	246
16	24	26	126
15	59	58	81
14	34	37	70
13	59	59	312
12	16	11	99
11	126	131	69
10	143	143	203
9	126	129	99
8	99	97	72
7	150	157	124
6	73	71	298
5	162	165	70
4	309	313	227
3	155	146	228
2	22	21	174
1	237	236	152
0	226	224	90

-5,-3,L

18	17	6	144
16	47	46	280
15	21	21	341
14	36	37	99
13	44	44	339
12	34	34	91
11	99	99	329
10	49	54	82
9	124	130	219
8	128	134	262
7	104	107	310
6	116	118	237
5	45	42	271
4	267	267	134
3	379	386	357
2	294	291	81
1	122	113	222
0	230	231	270

-5,-4,L

16	59	59	228
15	33	31	19
14	84	82	100
13	33	36	309
12	56	51	58
11	45	43	98
10	78	85	135
9	75	71	244
8	32	31	309
7	66	72	186
6	45	46	48
5	16	24	185
4	148	140	126
3	154	156	207
2	164	168	264
1	238	239	342
0	92	96	270

-5,-5,L

17	52	53	74
16	22	14	304
15	25	21	293
14	27	21	185
13	29	31	72
12	44	44	203
11	37	38	239
10	69	74	50
9	110	112	34
8	58	61	119
7	135	145	340
6	80	86	211
5	36	31	228
4	160	164	165
3	70	70	119
2	56	56	22
1	66	70	73
0	114	118	270

-5,-6,L

16	59	59	150
15	24	23	153
14	29	32	48
13	15	18	218
12	71	70	8
11	46	47	10
10	51	54	137
8	46	47	335
7	116	119	241
6	59	66	342
5	117	121	348
4	106	113	305
3	27	26	24
2	142	147	127
1	47	47	310
0	94	101	90

-5,-7,L

16	30	27	90
14	25	25	260
13	52	49	50
12	26	27	57
11	37	35	198
10	27	28	236
9	51	49	140
7	39	43	359
6	90	94	291
5	19	17	1
4	49	50	129
3	173	180	49
2	68	67	136
1	106	113	5
0	89	94	270

-5,-8,L

15	52	50	122
14	42	42	26
11	52	53	36
10	43	45	171
9	27	28	143
8	38	40	29
7	62	61	189
6	50	50	294
5	77	80	69
4	45	46	349
3	88	94	318
2	22	22	234

-5,-9,L

13	15	6	258
12	54	51	19
10	52	55	336
9	32	32	88
8	29	32	9
7	35	37	84
6	66	67	358
5	39	40	316
4	22	20	111
3	104	101	30
2	76	76	73
1	76	81	18
0	112	117	270

-5,-10,L

11	25	26	28
10	19	20	158
9	14	18	290
8	18	13	298
7	46	46	182
6	44	44	229
4	34	34	90
3	42	43	94
2	25	25	321
0	15	9	270

-5,-11,L

10	24	15	283
9	28	25	21
8	53	52	62

-5,-11,L

7	22	22	293
6	37	36	62
5	30	31	273
3	18	16	40
2	39	40	67
1	67	68	67
0	22	24	270

-5,-12,L

6	43	40	185
5	22	19	8
3	26	24	99
2	46	45	106
1	46	46	171
0	57	54	90

-5,-13,L

3	21	19	4
2	16	14	56
1	20	20	83
0	19	11	90

-6,0,L

17	99	90	270
16	23	19	0
15	49	46	270
14	98	103	180
13	48	46	270
12	47	41	0
11	54	53	270
9	32	38	90
8	49	44	0
7	265	268	270
6	152	154	0
5	149	158	90
3	103	112	90
2	359	376	0
1	113	113	270
0	294	292	180

-6,-1,L

18	19	7	274
16	32	34	288
14	34	31	95
13	52	53	74
12	15	21	131
11	19	17	59
10	143	152	105
9	39	44	162
8	258	271	68
7	111	118	30
6	24	24	317
5	107	108	247
4	112	111	109
3	238	233	199
2	198	193	127
1	240	240	343
0	164	159	0

-6,-2,L

18	38	36	72
17	68	66	273
15	60	57	18
13	42	40	175
12	55	59	288
11	41	40	270
10	77	79	319
9	23	24	60
8	56	54	70
7	137	140	279
6	114	113	315
5	77	75	295
4	200	205	34
3	216	216	192
2	138	143	141
1	208	214	345

-6,0,L

10	22	27	0

-6,-2,L

0	41	40	180

-6,-3,L

17	20	17	185
16	23	23	22
15	22	20	49
14	36	33	7
13	86	86	64
12	52	49	333
11	74	76	23
10	47	48	11
9	152	157	211
8	49	55	146
7	241	243	33
6	45	45	100
5	191	198	307
4	128	127	264
3	24	18	327
2	124	120	231
1	83	82	341
0	11	11	0

-6,-4,L

16	47	43	276
15	27	24	157
14	23	17	25
12	33	35	84
11	38	41	250
10	28	27	31
9	66	66	20
8	41	42	247
7	158	163	227
6	94	93	298
5	267	277	203
4	80	80	317
3	80	87	321
2	161	159	208
1	171	174	252
0	97	99	0

-6,-5,L

16	17	13	225
15	41	41	23
14	47	43	297
13	81	81	42
12	19	16	325
11	74	67	16
10	104	105	39
9	42	41	42
8	179	182	225
7	108	109	357
6	18	10	94
4	94	97	280
3	148	156	198
2	107	108	107
1	101	106	54
0	29	30	180

-6,-6,L

12	29	34	318
11	64	60	181
10	77	76	218
9	38	38	34
8	42	45	79
7	126	130	277
6	70	70	5
5	39	44	193
4	78	83	116
3	23	22	138
2	125	130	31
1	214	222	232
0	33	35	0

-6,-7,L

14	19	22	107
13	33	31	32
12	35	33	118
11	14	10	144
10	45	39	299
9	54	52	80
8	22	17	144
7	47	48	310
6	32	34	311
5	52	54	341
4	50	52	10
3	46	50	299
2	89	95	238
1	62	69	33
0	91	95	0

-6,-8,L

14	17	21	144
13	19	20	80
12	29	31	350
11	46	45	353
10	55	54	151
9	46	46	358
8	58	58	82
7	31	32	265
6	70	71	309
5	51	53	279
4	25	19	42
3	20	20	186
2	130	134	24
1	39	37	272

-6,-9,L

13	30	26	347
12	26	26	27
11	15	15	141
10	24	26	353
9	61	61	230

-6,-9,L

8	35	34	166
6	14	16	126
5	73	74	262
4	45	46	24
3	54	53	89
2	31	29	56
1	24	24	202
0	42	39	0

-6,-10,L

11	62	62	328
10	19	19	126
9	23	25	0
7	22	22	34
6	32	28	239
5	40	38	353
4	23	20	339
3	23	27	79
2	64	63	23
1	41	41	334
0	58	62	0

-6,-11,L

8	40	38	224
6	29	33	65
5	37	35	219
4	33	30	321
3	29	30	174
2	76	74	82
1	16	21	118

-6,-12,L

7	36	28	359
5	15	17	325
2	26	26	110

-6,-13,L

1	38	36	63

-7,0,L

17	46	46	270
16	38	35	180
15	82	78	270
13	84	86	90
12	50	52	0
11	66	63	270
10	97	97	180
9	200	212	90
8	15	11	0
7	19	21	270
6	72	73	0
5	91	93	270
2	97	102	180
1	31	37	270

-7,-1,L

16	64	62	293
15	36	38	145
14	49	50	265
13	47	47	184
12	54	57	265
11	20	23	18
10	56	52	259
9	66	68	312
8	87	94	11
7	148	158	174
6	151	157	202
5	150	158	17
4	102	101	157
3	139	147	190
2	43	51	112
1	113	119	165
0	66	65	270

-7,-2,L

17	16	12	302
15	34	34	280
14	40	39	326
13	20	21	263
12	56	53	80
11	107	109	323
10	52	54	273
9	92	95	96
8	111	114	103
7	89	89	65
6	127	134	333
5	126	127	283
4	62	60	238
3	96	103	75
2	67	66	331
1	151	150	162
0	80	85	90

-7,-3,L

17	25	25	197
16	27	32	268
15	23	22	278
14	27	30	98
13	25	23	202
12	32	32	202
10	19	19	242
9	95	97	170
8	133	136	288
7	54	53	117
6	170	175	227
5	153	151	350
4	48	38	126
3	138	138	171
2	63	65	284
1	127	126	175
0	134	138	270

-7,-4,L

16	24	25	298
15	65	68	293
14	94	94	61
13	33	33	6
12	90	92	53
11	17	14	275
10	86	84	331
9	27	29	314
8	69	72	334
7	73	76	170
6	115	120	21
5	157	167	262
4	75	79	287
3	102	101	146
2	68	70	351
1	62	64	282
0	18	19	90

-7,-5,L

16	28	28	158
15	30	30	259
14	28	27	43
13	31	28	225
12	51	50	152
11	19	15	295
10	31	32	28
9	40	42	110
8	30	29	29
7	41	41	214
6	88	98	203
5	40	41	258
4	106	106	274
3	145	149	177
2	157	169	248
1	53	57	67
0	220	225	270

-7,-6,L

15	51	51	267
14	46	43	322
13	37	36	87
12	58	52	14
11	38	39	323
9	24	22	320
8	62	62	34
7	63	62	292
6	54	55	357
5	35	35	266
4	142	147	275
3	75	75	237
2	87	90	107
1	113	118	205
0	13	18	90

-7,-7,L

14	28	32	91
13	34	32	354
11	26	29	160
10	62	62	346
9	72	73	189
8	43	43	354
7	24	27	181
6	86	85	229
5	35	36	0
4	29	31	226
2	74	78	217
1	15	17	102

-7,-8,L

13	20	15	252
12	40	42	101
11	31	29	306
10	33	34	210
9	41	40	224
8	42	40	167
7	15	8	192
6	64	61	266
5	35	39	30
4	52	54	182
3	51	51	359
2	13	14	69

-7,-8,L

1	66	64	71
0	18	16	270

-7,-9,L

12	21	20	7
11	32	33	131
10	26	27	6
9	31	32	125
8	29	25	313
7	37	36	116
4	59	57	15
3	18	20	133
1	18	26	351
0	37	36	270

-7,-10,L

9	33	29	253
8	16	11	233
6	20	21	246
5	51	52	307
4	28	30	186
3	29	25	36
1	60	63	27
0	38	38	90

-7,-11,L

8	22	22	3
7	24	28	229
6	16	15	187
5	39	41	202
2	25	20	194
1	33	30	53
0	24	19	270

-7,-12,L

4	20	22	288
3	16	17	97
1	26	25	134
0	52	47	90

-8,0,L

16	22	18	0
15	94	92	270
14	35	31	180
13	40	43	270
12	14	15	180
11	45	43	270
10	14	9	180
9	70	67	270
8	126	128	180
7	89	91	90
6	28	31	180
5	24	27	90
4	135	142	180
3	222	230	90
2	45	45	180
1	120	120	90
0	119	126	180

-8,-1,L

16	56	50	269
15	27	28	198
14	66	63	290
13	20	20	242
12	27	31	216
11	32	29	185
10	43	40	332
9	56	57	177
8	110	112	102
7	145	152	108
6	187	196	262
5	62	62	319
4	114	117	309
3	23	21	293
2	118	116	124
1	72	77	152
0	35	31	0

-8,-2,L

15	49	47	276
14	66	63	216
13	20	22	230
11	51	50	146
10	30	33	34
9	53	51	266
8	83	87	168
7	90	97	99
6	64	66	69
5	19	18	289
4	68	71	327
3	213	219	143
2	203	212	161
1	21	18	317
0	149	156	180

-8,-3,L

16	32	32	336
15	33	27	182
13	64	61	26
12	42	41	309
11	52	49	182
10	77	77	311
9	81	83	313
8	21	20	346
7	63	63	71
6	82	88	101
5	66	70	308
4	80	79	248
3	157	159	7
2	69	66	194
1	157	165	146
0	138	146	180

-8,-4,L

16	26	23	177
14	38	35	215
13	45	47	137
12	14	15	305
11	19	18	107
10	36	36	106
9	59	63	355
8	80	80	190
7	79	82	167
6	19	19	103
5	110	118	177
4	116	119	307
3	128	128	335
2	152	156	166
1	60	58	307
0	38	44	0

-8,-5,L

15	19	20	345
14	55	53	251
13	46	48	38
12	56	54	29
10	52	53	107
9	47	48	5
8	49	46	349
7	63	62	263
6	56	58	258
4	96	96	235
3	57	60	274
2	68	66	95
1	40	40	142
0	189	196	180

-8,-6,L

14	29	27	288
13	45	43	83
11	40	35	65
10	48	50	173
9	84	80	351
8	74	70	138
7	49	50	35
5	39	38	218
4	86	90	160
3	51	55	276
2	21	23	176
1	110	114	190
0	24	26	0

-8,-7,L

10	71	71	239
9	37	33	139
8	15	18	340
7	20	19	70
6	53	50	273
5	41	45	242
4	28	23	351
3	70	67	260
2	24	25	328
0	29	27	180

-8,-8,L

12	28	33	46
11	47	45	73
10	41	41	120
9	39	38	326
8	27	27	186
7	52	51	114
6	38	35	76
5	31	34	317
4	53	51	210
3	23	16	146
2	38	33	206
1	28	27	265
0	110	110	180

-8,-9,L

10	37	35	256
9	39	38	218
8	21	22	288

-8,-9,L

7	22	24	177
6	33	33	3
5	63	62	226
4	20	21	307
3	49	50	139
2	24	25	37
1	51	51	96
0	29	35	0

-8,-10,L

9	17	9	15
8	33	37	226
7	37	35	205
6	49	47	162
5	23	21	111
4	26	24	272
1	43	43	51
0	26	28	0

-8,-11,L

4	28	31	305
3	27	23	200
2	48	47	77
1	29	32	143
0	29	31	0

-8,-12,L

1	23	23	134

-9,0,L

15	29	27	270
14	44	44	180
13	31	29	270
12	33	38	180
10	79	79	180
8	16	14	180
7	70	78	270
6	24	22	180
5	63	66	270
4	172	177	0
3	150	156	270
2	19	20	180
1	116	123	90

-9,-1,L

15	30	27	178
14	65	64	260
13	27	24	241
12	21	17	177
11	43	43	358
9	39	38	168
8	16	21	78
7	21	26	202
6	86	92	112
5	75	77	261
4	124	129	128
3	99	102	296
2	124	130	95
1	75	78	144
0	39	36	90

-9,-2,L

15	41	37	0
14	39	39	243
13	58	58	280
12	28	23	225
11	41	43	14
9	18	17	287
8	87	89	146
7	37	32	55
6	47	46	190
5	93	95	215
4	69	72	47
3	38	44	173
2	54	60	188
1	137	140	144
0	136	148	90

-9,-3,L

15	32	31	236
14	40	34	221
13	37	39	257
11	25	26	304
9	54	53	168
8	41	39	79
7	35	33	40
6	130	131	107
5	93	87	338
4	46	46	88
3	46	46	10
2	41	48	32
1	68	67	143
0	135	136	90

-9,-4,L

14	34	36	86
13	31	26	264
12	36	34	179
11	60	61	82
9	42	44	15
8	67	66	250
7	25	31	111
6	39	39	127
5	40	43	259
4	49	49	329
3	37	37	39
2	32	34	114
1	129	131	162
0	33	40	90

-9,-5,L

13	28	23	229
12	71	71	91
11	51	52	34
10	40	42	24
9	36	37	141
8	38	37	25
7	43	40	60
6	61	63	78
5	50	52	148
4	24	27	301
3	18	17	343
2	14	11	295
1	26	29	24
0	18	9	90

-9,-6,L

12	40	42	228
11	17	20	133
10	28	25	107
9	26	21	45
8	21	24	69
7	58	59	338
6	20	22	180
5	26	23	142
4	73	74	267
3	50	53	301
2	33	33	332
1	48	50	130
0	33	37	90

-9,-7,L

12	20	22	99
11	63	62	71
10	59	56	15
9	41	42	132
7	34	39	101
6	36	34	71
5	21	20	22
4	35	38	216
3	55	57	276
2	36	32	275
1	66	65	185
0	40	42	90

-9,-8,L

11	41	41	203
10	17	13	9
9	24	21	220
8	37	30	168
7	37	33	2
6	45	40	215
5	24	22	25
4	66	67	177
3	20	18	14
2	27	24	187
1	46	45	44
0	34	35	90

-9,-9,L

10	32	25	79
6	40	37	139
5	33	32	86
4	14	16	40
3	19	18	155
2	24	28	326
1	21	17	212
0	49	44	90

-9,-10,L

5	19	25	291
2	30	22	162
1	26	24	60
0	31	35	90

-9,-11,L

4	31	29	122
3	30	25	285
2	28	27	131
1	35	34	293
0	48	51	90

-10,0,L

11	35	35	270
10	34	37	0
9	28	24	270
7	26	30	90
5	18	12	270
4	61	60	0
3	36	36	90
2	90	96	0
1	97	97	90
0	55	55	0

-10,-1,L

15	18	19	17
14	48	47	324
13	63	61	217
12	25	21	113
11	33	28	18
10	57	54	39
9	75	72	179
8	95	97	195
7	43	44	152
6	61	63	214
5	78	77	350
4	27	28	328
3	20	15	7
2	39	44	124
1	16	19	74
0	43	39	180

-10,-2,L

14	30	29	256
13	41	41	284
12	46	44	314
11	19	19	179
10	19	5	251
9	38	35	37
8	35	36	268
7	46	46	53
6	39	36	28
5	110	109	70
4	136	139	310
3	14	16	121
2	68	72	353
1	23	26	288
0	25	27	180

-10,-3,L

13	25	28	229
12	24	24	246
11	40	42	205
10	66	64	35
9	46	49	352
8	18	20	357
7	80	77	198
6	31	35	112
5	34	35	90
4	34	33	223
3	31	31	350
2	86	93	181
1	37	41	107
0	151	151	180

-10,-4,L

13	19	20	178
12	47	45	309
11	56	56	351
10	15	10	344
9	25	22	72
8	18	19	41
7	15	14	285
5	109	106	87
4	77	76	338
3	70	68	307
2	49	44	32
1	74	78	46

-10,-5,L

13	20	21	217
12	16	18	81
11	31	29	218
10	59	58	115
9	18	16	95
8	89	91	18
7	50	50	193
6	38	36	287
5	28	29	120
4	50	49	99
3	29	26	332
2	37	39	68
1	34	33	54
0	59	61	180

-10,-6,L

12	23	24	89
10	75	72	46
8	77	72	91
7	49	49	26
6	21	23	21
4	51	51	45
3	80	80	270
2	41	39	300
1	45	44	78
0	17	14	180

-10,-7,L

11	26	32	356
10	46	46	150
9	21	17	94
8	31	35	83
7	33	31	37
6	19	21	16
5	19	23	246
4	44	40	48
3	22	30	194
2	66	66	9
1	30	32	39
0	15	15	0

-10,-8,L

10	43	42	26
7	32	30	128
6	58	55	70
4	35	34	356
3	33	31	269
2	43	46	259
1	57	53	306
0	14	15	180

-10,-9,L

8	35	33	44
7	20	18	158
6	44	41	2
4	18	16	130
3	31	34	199
2	16	20	161
1	26	25	27

-10,-10,L

5	36	37	147
4	29	25	324
3	20	9	50
1	51	52	88
0	32	28	0

-11,0,L

13	17	11	270
12	21	21	180
11	47	39	90
8	30	27	180
7	44	44	270
4	81	81	0
3	45	44	90
2	41	39	0
1	48	52	90

-11,-1,L

12	46	45	274
11	29	27	230
9	15	15	42
8	22	16	256
7	32	30	309
6	81	81	359
5	57	60	287
4	34	34	349
3	106	107	320
1	66	69	354
0	51	51	270

-11,-2,L

12	35	32	283
11	23	24	59
10	18	18	21
9	22	24	356
8	26	21	209
6	60	57	213
5	31	29	183
4	28	23	316
3	38	40	174
2	33	31	267
1	68	66	224
0	46	45	90

-11,-3,L

13	38	35	338
12	51	48	312
11	49	44	269
10	53	51	315
8	31	28	47
7	66	64	200
6	52	52	18
5	40	40	310
4	50	48	328
3	73	72	358

-11,-3,L

2	63	62	308

-11,-4,L

12	32	34	250
9	21	24	60
8	25	26	307
7	29	28	302
6	29	28	129
4	57	57	51
3	34	36	61
2	32	32	2
1	53	58	194
0	53	53	270

-11,-5,L

12	15	18	79
11	16	13	19
10	31	30	292
9	46	46	11
7	20	18	78
6	22	26	329
4	61	58	265
3	20	20	350
2	56	55	316
1	42	40	236
0	25	24	270

-11,-6,L

11	24	23	167
10	27	26	20
9	62	58	80
8	41	42	23
7	26	25	3
4	22	21	51
3	58	55	85
2	46	42	17
1	29	28	56
0	73	73	90

-11,-7,L

9	40	37	28
8	27	23	178
7	35	31	127
6	23	22	16
5	44	48	16
4	51	50	253
3	56	54	302
2	30	29	329
1	28	28	258
0	35	32	270

-11,-8,L

8	27	28	39
7	47	47	47
6	33	36	164
5	25	26	20
3	30	27	105
1	41	38	308
0	29	26	90

-11,-9,L

5	50	48	49
4	21	20	195
3	16	11	337
2	23	22	354
0	18	11	90

-12,0,L

12	27	27	180
11	17	22	270
8	16	6	0
7	15	14	90
6	16	10	180
5	37	33	270
1	19	13	90
0	30	34	0

-12,-1,L

12	19	17	176
11	19	12	34
10	17	11	13
9	39	36	165
8	88	85	246
7	55	51	254
6	25	25	50
5	47	47	199
4	16	13	50
3	21	18	331
2	25	23	33
1	20	19	35

-12,-2,L

12	33	29	325
11	17	20	268
10	49	51	188
9	29	26	15
8	19	24	178
7	30	31	359
6	46	44	187
5	57	56	352
4	29	26	234
3	78	76	326
2	49	48	359
1	52	53	253
0	18	12	180

-12,-3,L

11	24	16	275
10	26	26	21
9	47	44	21
8	18	11	280
7	36	35	275
6	40	34	282
5	46	44	64
4	19	19	290
3	38	33	353
2	35	32	211
1	61	59	311

-12,-4,L

11	53	50	336
10	31	33	235
7	17	19	322
6	62	62	230
5	51	52	314
4	40	32	201
3	68	60	277
2	56	52	299
1	46	43	289
0	87	87	180

-12,-5,L

9	51	47	5
8	18	18	11
7	36	33	36
6	27	24	249
5	21	16	158
4	43	39	86
3	58	57	26
2	51	48	124
1	15	16	2
0	30	31	0

-12,-6,L

9	38	40	199
8	18	17	68
7	22	20	66
6	20	18	222
5	62	59	293
4	17	17	35
3	24	23	256
2	30	31	267
1	52	48	337
0	72	69	180

-12,-7,L

7	31	31	18
6	44	44	49
3	38	33	18
2	24	19	91
1	22	23	98
0	27	23	0

-12,-8,L

5	29	28	220
4	26	28	16
3	15	11	77
2	22	27	253
1	32	31	342

-13,0,L

9	60	61	270
8	56	52	180
7	61	58	270
4	83	80	180
3	40	42	90
2	17	14	0

-13,-1,L

10	38	34	121
9	38	36	188
8	25	25	105
6	50	46	33
5	53	51	167
4	40	38	6
3	51	51	195
2	16	15	211
0	39	39	90

-13,-2,L

8	21	21	197
7	35	33	263
6	24	26	195
5	31	30	8
4	41	41	192
3	30	26	265
2	58	54	23
1	26	27	281
0	24	23	270

-13,-3,L

9	34	31	178
7	38	36	205
6	39	36	292
5	33	33	194
4	36	38	354
2	33	31	258
1	21	21	241
0	28	25	90

-13,-4,L

8	31	28	16
7	22	22	244
6	27	23	9
4	35	31	90
2	59	56	2
1	48	48	34
0	74	75	270

-13,-5,L

8	28	23	102
5	43	40	240
4	37	34	321
2	40	42	289
1	48	47	234
0	21	24	270

-13,-6,L

6	38	37	340
4	15	7	128
3	41	41	154
2	22	23	9
1	42	39	91

-13,-7,L

4	27	17	343
2	33	32	78
1	30	34	225
0	17	19	90

-14,0,L

8	16	13	180
7	28	27	90
5	25	26	90
4	48	47	180
2	92	86	180
1	36	35	90
0	73	71	0

-14,-1,L

8	36	36	278
7	37	35	195
6	35	33	314
5	72	69	176
2	25	21	310
1	20	18	51
0	17	15	180

-14,-2,L

7	18	15	128
4	16	19	125
3	20	22	345
2	33	27	187
1	62	58	145
0	36	33	0

-14,-3,L

6	18	19	254
5	20	17	54
4	48	44	116
3	26	25	96
2	21	18	315
1	57	58	328
0	28	25	0

-14,-4,L

6	16	20	296
5	23	22	338
4	27	27	268
3	27	23	17
2	45	46	301
0	19	14	0

-14,-5,L

4	22	19	95
3	28	25	117
2	27	22	101
1	39	39	297
0	46	46	0

-15,0,L

4	29	27	180
3	21	20	90
2	18	12	180
1	31	28	270

-15,-1,L

4	40	37	266
3	39	38	197
2	28	26	141
1	22	18	356

-15,-2,L

3	23	19	149
1	15	15	222
0	45	43	270

-15,-3,L

2	35	32	98
1	24	22	344
0	25	25	90

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CHAPTER THREE

An x-ray analysis of two derivatives of 2-naphthol

3.1 Introduction

Substituents in the 1,8-or 4, 5- positions in naphthalene (I) cause greater steric hindrance than if they were ortho (e.g. 1, 2-). The interactions resulting from this type of substitution are known as peri-interactions and have been the subject of a comprehensive review (1).

The effect of peri-strain on the autoxidation of 1-alkyl-2- naphthols has recently been reported by Brady and Carnduff (2). This reaction shows the characteristics of a radical chain process and occurs in the presence of atmospheric oxygen.

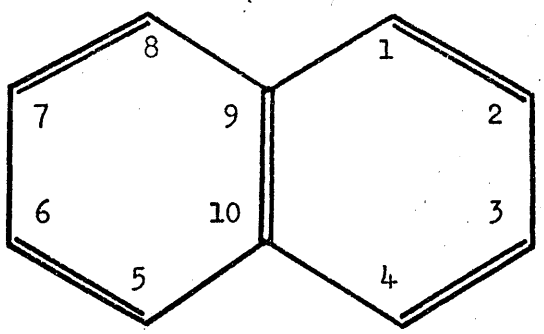
Brady and Carnduff found that the relative times for the uptake of a given quantity of oxygen were as follows:

$$A \text{ (inert)} = B \gg C > D \gg E \text{ (Fig. 3.1).}$$

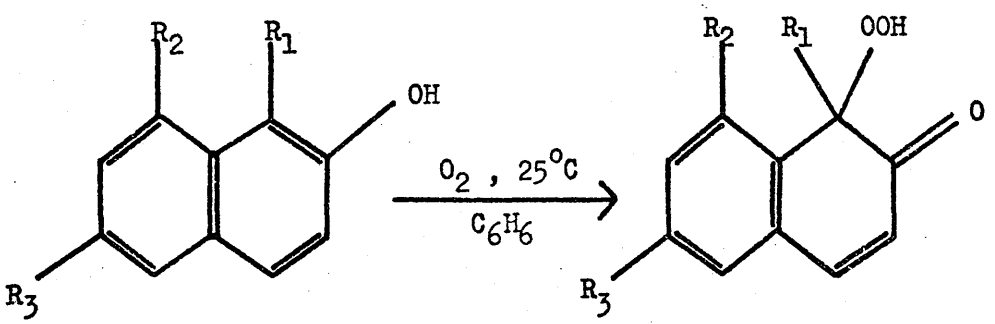
These reaction rates correlate with the increasing strain in the peri-positions and may possibly be accounted for by the relief in steric hindrance when C(1) becomes tetrahedral.

Dr. J. Carnduff (University of Glasgow) supplied two of a series of derivatives of 2-naphthols for the following x-ray analyses. These analyses form part of a study to assess the relative strain in a number of compounds in which R_1, R_2, R_3 (Fig. 3.1) are allowed to vary.

The crystal structure analyses could not easily be carried out on the 2-naphthols themselves since the autoxidation occurs at room temperature in the presence of molecular oxygen. The 2-hydroxyl group was therefore



(I)



	R_1	R_2	R_3
A	Me	H	H
B	Me	H	Bu^t
C	Pr^i	H	H
D	Me	Me	H
E	Bu^t	H	H

Fig. 3.1 Autoxidation of 1-alkyl-2-naphthols

protected by acetylation; it being assumed that this substitution would have a minimal effect on strain elsewhere in the molecule.

3.2 1—Methyl—2—naphthyl-acetate

Experimental

Crystal Data

1—Methyl—2—naphthyl-acetate: $C_{13}H_{12}O_2$

Unit cell dimensions $\underline{a}$ = 6.455 A^o α = 90.0°

$\underline{b}$ = 8.325 A^o β = 91.95°

$\underline{c}$ = 20.252 A^o γ = 90.0°

Space group $P2_1/C$ (C_2^5h)

M = 200 a.m.u.

V = 1088 A^{o3}

Do= 1.41 $gm.cm^{-3}$

Dc= 1.222 $gm.cm^{-3}$

μ = 0.88 cm^{-1} (Mo-Kα)

F(000) = 424

Z = 4

The space group was uniquely determined by the systematic absences:

hOl when l = 2n, OkO when k = 2n.

The crystal used in this analysis was a small cube of side 1mm.

Data Collection

Precession photographs were used to measure the cell dimensions and to determine the space group. The crystal was then mounted and aligned on the goniometer head of the Hilger diffractometer as described previously. The cell dimensions quoted in the crystal data are those computed during this diffractometer setting up procedure.

The $\theta, 2\theta$ scanning technique was used to obtain intensity data from zirconium filtered Mo-Kα radiation. The scan parameters were as follows:

Increment in θ	0.02°
Number of scan steps	40
Time per step	1 sec.

The background count was measured for 20 seconds immediately before and after each peak count. The intensities of two strong reflexions were checked after every 40 intensity measurements and no significant variation in their values was recorded.

These standards were used to place the measured intensities for the hkl and $hk\bar{l}$ octants ($2\theta < 52^{\circ}$) on a common scale.

The integrated intensities (I) were reduced to 1682 independant structure amplitudes by exclusion of the data for which $I < 2\sigma I$.

Reduced beam intensity was employed to remeasure the reflexions for which $2\theta < 12^{\circ}$ in order to correct for counter saturation errors.

No absorption correction was applied.

Structure Analysis

The structure was elucidated by the direct phase determining program MULTAN. Triplet relationships were derived for the largest 200 of the normalised structure factors ($|E| \geq 1.45$).

The starting set of 7 reflexions (3 origin defining, Table I) was selected by the program on the basis that phases with a probability in excess of 0.95[$] were acceptable. Sixteen phase sets were then calculated for the 200 reflexions with the largest value of $|E|$ and an E-map computed from the set showing the highest combined figure of merit revealed all the non-hydrogen atoms.

A structure factor calculation using these co-ordinates gave an R of 45.8%. The carbon and oxygen atom locations were then refined with a full matrix least squares procedure, using the 1508 independant structure amplitudes for which $|F| \geq 7\sigma(|F|)$, and the calculations converged at R = 26.1% (isotropic vibration) and R = 15.6% (anistropic thermal motion).

After making allowance for errors caused by counter saturation R was reduced to 12.2%. Subsequent difference syntheses were used to obtain co-ordinates for all the hydrogen atoms and when these atoms were allowed to assume isotropic vibration R fell to 5.1%

A weighting scheme of the form:

$$W = 1/(A + BFo + CFo^2) \text{ with } A=0.1728,$$

$$B=-0.0277 \text{ and } C=0.035$$

was applied. The values of the constants A, B and C

TABLE I SUMMARY OF STRUCTURE DETERMINATION

A. INITIAL SET OF PHASES

REFLECTION				PHASE *	MOD. E
2	5	-13	+	360	4.90
2	7	4	+	360	3.43
1	2	2	+	360	3.21
3	6	-12		360 OR 180	4.14
3	5	6		360 OR 180	3.51
1	4	-15		360 OR 180	3.15
4	2	-9		360 OR 180	2.94

B. STATISTICS

	E1	E2	E3	E4	E5	E6
THEORETICAL FOR CENTRIC	0.798	1.00	0.968	31.73	4.55	0.27
THEORETICAL FOR ACENTRIC	0.886	1.00	0.736	36.79	1.83	0.01
FOUND	0.803	1.00	0.991	27.80	5.00	0.9

* IN DEGREES
\+ ORIGIN DEFINING

MOD. E MODULUS OF E FOR REFLECTION CONCERNED
E1 MEAN VALUE FOR MODULUS OF E
E2 MEAN VALUE FOR MODULUS OF E**2
E3 MEAN VALUE FOR MODULUS OF ((E**2)-1)
E4 % OF REFLECTIONS WITH MODULUS OF E >1.0
E5 % OF REFLECTIONS WITH MODULUS OF E >2.0
E6 % OF REFLECTIONS WITH MODULUS OF E >3.0

were chosen so that the deviation from constant $\underline{w\Delta^2}$ over the range of $|F_o|$ and $\sin\theta$ was minimised.

The refinement then converged at $\underline{R} = 4.6\%$.

No correction was made for absorption.

3.3 Results

Table II 1-Methyl-2-naphthyl acetate: Fractional atomic coordinates

Positional estimated standard deviations are shown in parentheses.

The hydrogen atoms are numbered according to the atoms to which they are attached.

The table shows:

Atom	x	y	z

C(1)	5324(3)	0779(2)	1196(1)
C(2)	4623(3)	1732(2)	0693(1)
C(3)	2786(3)	2624(2)	0705(1)
C(4)	1639(3)	2581(2)	1253(1)
C(5)	1146(4)	1637(3)	2398(1)
C(6)	1824(4)	0766(3)	2933(1)
C(7)	3635(4)	-0127(3)	2903(1)
C(8)	4743(4)	-0150(2)	2346(1)
C(9)	4134(3)	0752(2)	1784(1)
C(10)	2288(3)	1658(2)	1810(1)
C(11)	7228(4)	-0215(3)	1137(1)
C(12)	6982(3)	3031(2)	0006(1)
C(13)	7935(6)	2922(4)	-0653(1)
O(14)	5717(2)	1770(2)	0102(1)
O(15)	7262(2)	4061(2)	0405(1)
H(3)	2445(30)	3273(25)	0338(10)
H(4)	0344(36)	3142(27)	1287(10)
H(5)	-0098(37)	2208(29)	2391(11)
H(6)	1038(35)	0785(27)	3324(12)
H(7)	4176(37)	-0722(29)	3296(13)
H(8)	6064(40)	-0748(31)	2325(12)
H(111)	8170(46)	-0041(35)	1474(15)
H(112)	7885(37)	-0055(28)	0720(13)
H(113)	6816(48)	-1414(38)	1180(14)
H(131)	8219(47)	1878(42)	-0761(14)
H(132)	9153(68)	3526(50)	-0656(19)
H(133)	6932(60)	3298(45)	-0976(19)

Table III 1-Methyl-2-naphthyl acetate: Thermal parameters

Carbon and oxygen values are anisotropic.

Hydrogen values are isotropic.

Estimated errors in the last digit are shown in parentheses.

All figures are multiplied by 10^3

The anisotropic temperature factor expression used was of the form described by equation (12) in chapter one, the coefficients being in terms of the mean square amplitudes of vibration U_{ij} .

The table shows:

Atom	U_{11} or U	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}

C(1)	68(1)	50(1)	55(1)	-4(1)	5(1)	-3(1)
C(2)	83(1)	50(1)	49(1)	-8(1)	9(1)	-5(1)
C(3)	97(1)	57(1)	58(1)	6(1)	1(1)	6(1)
C(4)	79(1)	63(1)	72(1)	12(1)	3(1)	0(1)
C(5)	84(1)	60(1)	85(1)	-4(1)	25(1)	-7(1)
C(6)	118(2)	66(1)	63(1)	-17(1)	36(1)	-1(1)
C(7)	116(2)	71(1)	58(1)	-5(1)	13(1)	10(1)
C(8)	87(1)	66(1)	63(1)	0(1)	5(1)	8(1)
C(9)	68(1)	48(1)	54(1)	-9(1)	7(1)	-2(1)
C(10)	73(1)	48(1)	59(1)	-6(1)	7(1)	-3(1)
C(11)	70(1)	86(2)	73(1)	7(1)	11(1)	5(1)
C(12)	79(1)	60(1)	55(1)	2(1)	9(1)	10(1)
C(13)	125(2)	93(2)	72(2)	-9(2)	36(2)	4(1)
O(14)	111(1)	62(1)	51(1)	-14(1)	21(1)	-5(1)
O(15)	102(1)	69(1)	68(1)	-16(1)	12(1)	-5(1)
H(3)	39(5)					
H(4)	52(6)					
H(5)	53(6)					
H(6)	56(6)					
H(7)	63(7)					
H(8)	65(7)					
H(111)	80(9)					
H(112)	58(7)					
H(113)	93(10)					
H(131)	85(10)					
H(132)	115(14)					
H(133)	108(13)					

TABLE IV

1-METHYL-2-NAPHTHYL ACETATE:
INTRAMOLECULAR BONDED DISTANCES(ANGSTROMS)
STANDARD DEVIATIONS (ANGSTROMS) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	DIST.	ATOM1	ATOM2	DIST.
C1	C2	1.356(2)	C12	O14	1.349(2)
C1	C9	1.439(2)	C12	O15	1.188(2)
C1	C11	1.490(2)	C3	H3	0.939(20)
C2	C3	1.400(2)	C4	H4	0.962(23)
C2	O14	1.409(2)	C5	H5	0.932(24)
C3	C4	1.355(2)	C6	H6	0.954(23)
C4	C10	1.417(2)	C7	H7	0.990(25)
C5	C6	1.363(3)	C8	H8	0.990(26)
C5	C10	1.421(2)	C11	H111	0.909(30)
C6	C7	1.388(3)	C11	H112	0.966(25)
C7	C8	1.357(3)	C11	H113	1.037(31)
C8	C9	1.406(2)	C13	H131	0.916(34)
C9	C10	1.413(2)	C13	H132	0.933(43)
C12	C13	1.491(3)	C13	H133	0.956(38)

TABLE V 1-METHYL-2-NAPHTHYL ACETATE: SOME INTRAMOLECULAR NON-BONDED SEPARATIONS

ATOM1	ATOM2	DIST #	ATOM1	ATOM2	DIST #
C(1)	C(8)	2.494	O(15)	H(112)	3.51
C(11)	O(14)	2.817	H(4)	H(5)	2.39
C(11)	H(8)	2.58	H(7)	H(8)	2.35
O(15)	H(3)	3.18	H(8)	H(111)	2.31

IN ANGSTROMS

TABLE VI 1-METHYL-2-NAPHTHYL ACETATE: INTERMOLECULAR CONTACTS OF LESS THAN 3.85 ANGSTROMS

ATOM1	ATOM2		DIST #	ATOM1	ATOM2		DIST #
C(11)	C(4)	*	3.680	C(12)	O(15)	***	3.729
O(15)	C(4)	*	3.482	O(15)	O(15)	***	3.652
O(15)	C(3)	*	3.791	C(5)	C(8)	****	3.791
C(1)	O(14)	**	3.427	C(9)	C(7)	****	3.767
C(2)	O(14)	**	3.334	C(10)	C(7)	****	3.785
C(11)	O(14)	**	3.356	C(10)	C(8)	****	3.665
C(3)	C(13)	***	3.740	O(15)	C(6)	****	3.682
C(3)	O(15)	***	3.559	O(15)	C(7)	****	3.560

IN ANGSTROMS

THE ASTERISKS(*) REFER TO THE FOLLOWING TRANSFORMATIONS OF THE ATOMIC COORDINATES

*	1.0+X, Y, Z
**	1.0-X, -Y, -Z
***	1.0-X, 1.0-Y, -Z
****	-X,-0.5+Y,-0.5-Z

TABLE VII

1-METHYL-2-NAPHTHYL ACETATE: VALENCY ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ANGLE	ATOM1	ATOM2	ATOM3	ANGLE
C9	C1	C2	117.2(1)	C11	C1	C2	121.3(1)
C11	C1	C9	121.5(1)	O14	C2	C1	119.1(1)
C3	C2	C1	123.9(1)	O14	C2	C3	116.9(1)
C4	C3	C2	119.2(1)	C10	C4	C3	120.8(1)
C10	C5	C6	120.6(2)	C7	C6	C5	119.9(2)
C8	C7	C6	120.8(2)	C9	C8	C7	121.6(2)
C10	C9	C1	119.8(1)	C8	C9	C1	122.3(1)
C10	C9	C8	117.9(1)	C5	C10	C4	121.7(1)
C9	C10	C4	119.1(1)	C9	C10	C5	119.1(1)
O14	C12	C13	110.7(1)	O15	C12	C13	126.5(2)
O15	C12	O14	122.8(1)	C12	O14	C2	117.6(1)
H3	C3	C2	117.9(12)	H3	C3	C4	122.9(12)
H4	C4	C3	123.1(12)	H4	C4	C10	116.1(12)
H5	C5	C6	122.5(13)	H5	C5	C10	116.8(13)
H6	C6	C5	118.9(13)	H6	C6	C7	121.2(13)
H7	C7	C6	120.5(14)	H7	C7	C8	118.6(14)
H8	C8	C7	121.4(14)	H8	C8	C9	116.9(14)
H111	C11	C1	112.6(18)	H112	C11	C1	112.4(14)
H113	C11	C1	108.3(17)	H112	C11	H111	109.3(23)
H113	C11	H111	104.9(24)	H113	C11	H112	109.2(21)
H131	C13	C12	111.3(18)	H132	C13	C12	110.3(24)
H133	C13	C12	107.5(23)	H132	C13	H131	109.5(32)
H133	C13	H131	106.5(29)	H133	C13	H132	111.8(34)

TABLE VIII

1-METHYL-2-NAPHTHYL ACETATE: TORSION ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
C9	C1	C2	C3	-2.7(2)	C9	C1	C2	O14	-178.7(1)
C11	C1	C2	C3	176.4(1)	C11	C1	C2	O14	0.4(2)
C2	C1	C9	C8	-177.9(1)	C2	C1	C9	C10	1.9(2)
C11	C1	C9	C8	3.0(2)	C11	C1	C9	C10	-177.2(1)
C1	C2	C3	C4	1.6(3)	O14	C2	C3	C4	177.7(1)
C1	C2	O14	C12	-101.2(1)	C3	C2	O14	C12	82.5(2)
C2	C3	C4	C10	0.5(3)	C3	C4	C10	C5	177.9(1)
C3	C4	C10	C9	-1.2(2)	C10	C5	C6	C7	-0.7(3)
C6	C5	C10	C4	-178.6(2)	C6	C5	C10	C9	0.5(3)
C5	C6	C7	C8	-0.2(3)	C6	C7	C8	C9	1.5(3)
C7	C8	C9	C1	178.1(1)	C7	C8	C9	C10	-1.7(2)
C1	C9	C10	C4	0.0(2)	C1	C9	C10	C5	-179.1(1)
C8	C9	C10	C4	179.8(1)	C8	C9	C10	C5	0.7(2)
C13	C12	O14	C2	-177.3(1)	O15	C12	O14	C2	2.9(2)
C2	C1	C11	H111	126.3(20)	C2	C1	C11	H112	2.4(16)
C2	C1	C11	H113	-118.2(17)	C9	C1	C11	H111	-54.6(20)
C9	C1	C11	H112	-178.5(15)	C9	C1	C11	H113	60.9(17)
C1	C2	C3	H3	178.3(13)	O14	C2	C3	H3	-5.6(14)
C2	C3	C4	H4	-178.2(16)	H3	C3	C4	C10	-176.1(14)
H3	C3	C4	H4	5.3(21)	H4	C4	C10	C5	-3.4(15)

TORSION ANGLES (CONTINUED)

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
C4	C4	C10	C9	177.5(15)	C10	C5	C6	H6	179.1(15)
C5	C5	C6	C7	176.7(17)	H5	C5	C6	H6	-3.5(23)
C5	C5	C10	C4	3.9(16)	H5	C5	C10	C9	-177.1(16)
C6	C6	C7	H7	177.1(16)	H6	C6	C7	C8	180.0(16)
C6	C6	C7	H7	-2.7(23)	C6	C7	C8	H8	177.6(17)
C7	C7	C8	C9	-175.9(16)	H7	C7	C8	H8	0.2(23)
C8	C8	C9	C1	1.8(16)	H8	C8	C9	C10	-178.0(16)
O14	C12	C13	H131	-36.0(21)	O14	C12	C13	H132	-157.7(27)
O14	C12	C13	H133	80.2(24)	O15	C12	C13	H131	143.7(21)
O15	C12	C13	H132	22.0(27)	O15	C12	C13	H133	-100.0(24)

THE ANGLE 1-2-3-4 IS DEFINED AS POSITIVE IF,WHEN VIEWED ALONG THE 2-3 BOND,ATOM 1 HAS TO BE ROTATED CLOCKWISE TO ECLIPSE ATOM 4

TABLE IX 1-METHYL-2-NAPHTHYL ACETATE: MEAN PLANES CALCULATIONS

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
1.	C(1)		-0.012(2)
	C(2)		0.031(2)
	C(3)		0.013(2)
	C(4)		-0.016(2)
	C(5)		-0.004(2)
	C(6)		0.021(2)
	C(7)		0.018(2)
	C(8)		-0.016(2)
	C(9)		-0.017(2)
	C(10)		-0.019(2)
		C(11)	-0.071(3)
		O(14)	0.010(1)
		H(4)	-0.056(23)
		H(5)	-0.051(25)
		H(8)	0.018(26)

TABLE IX (CONTINUED)

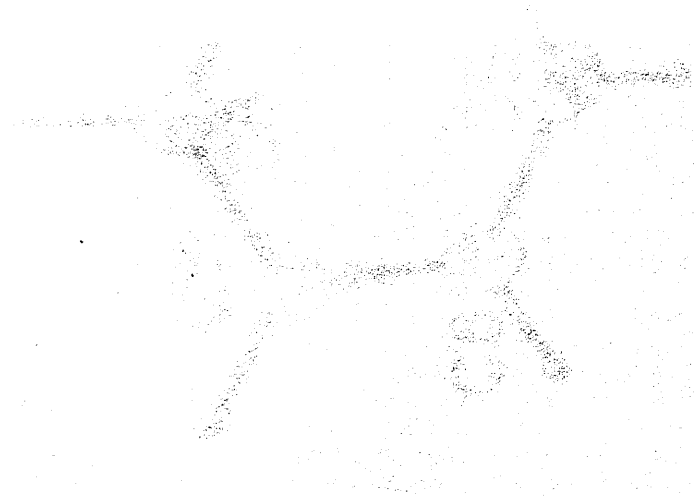
	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
2.	C(12)		0.000(2)
	C(13)		0.000(4)
	C(14)		0.000(1)
		O(15)	0.004(2)

THE OUT OF PLANE ATOMS WERE NOT INCLUDED IN THE DERIVATION OF THE PLANES.

THE EQUATIONS OF THESE PLANES ARE:

1. $0.5113X + 0.7815Y + 0.3576Z = 3.0991$
2. $0.7539X - 0.5148Y + 0.4082Z = 2.1024$

Fig. 3.2 1-Methyl-2-naphthyl acetate: A view of the molecule



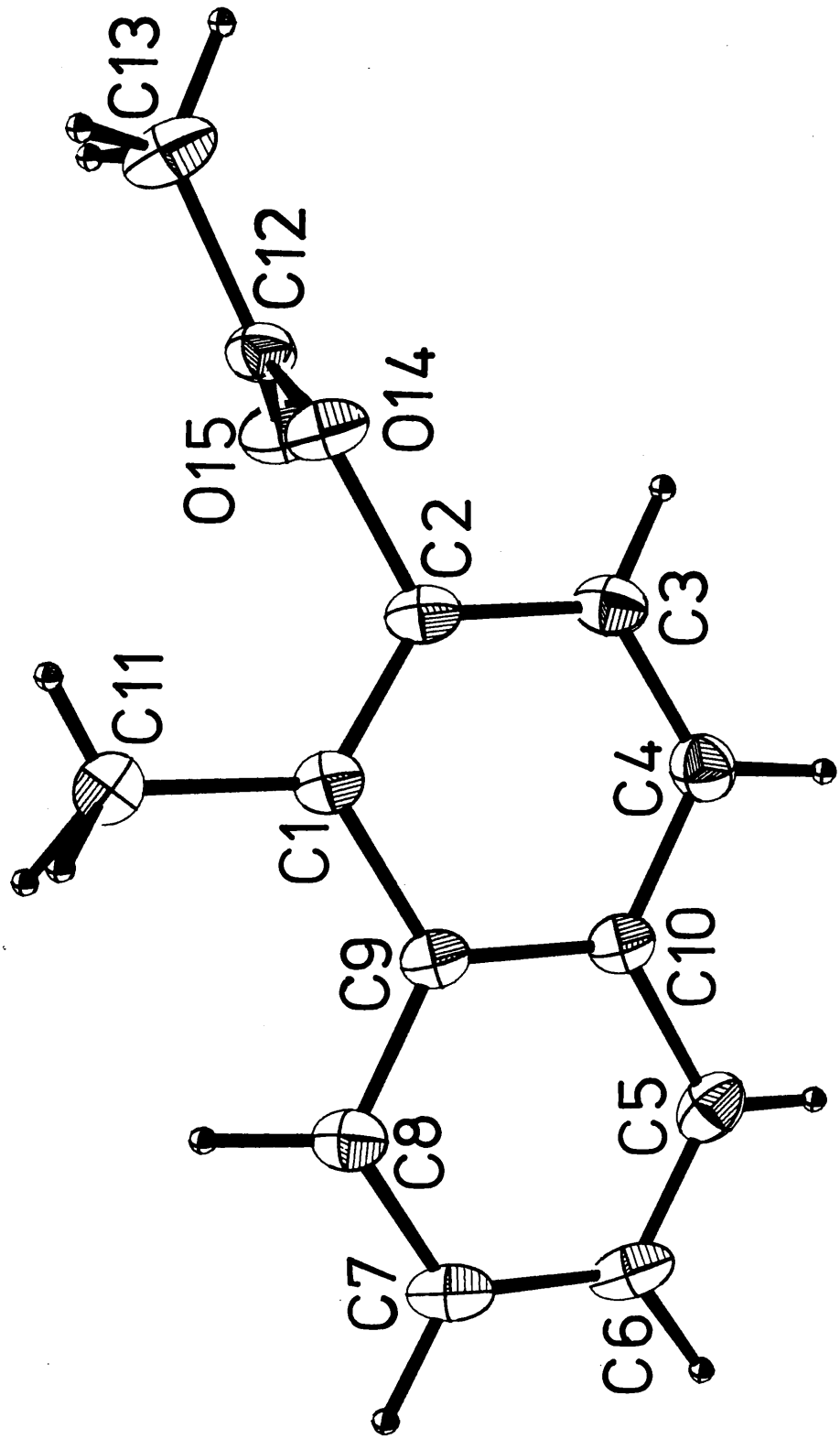
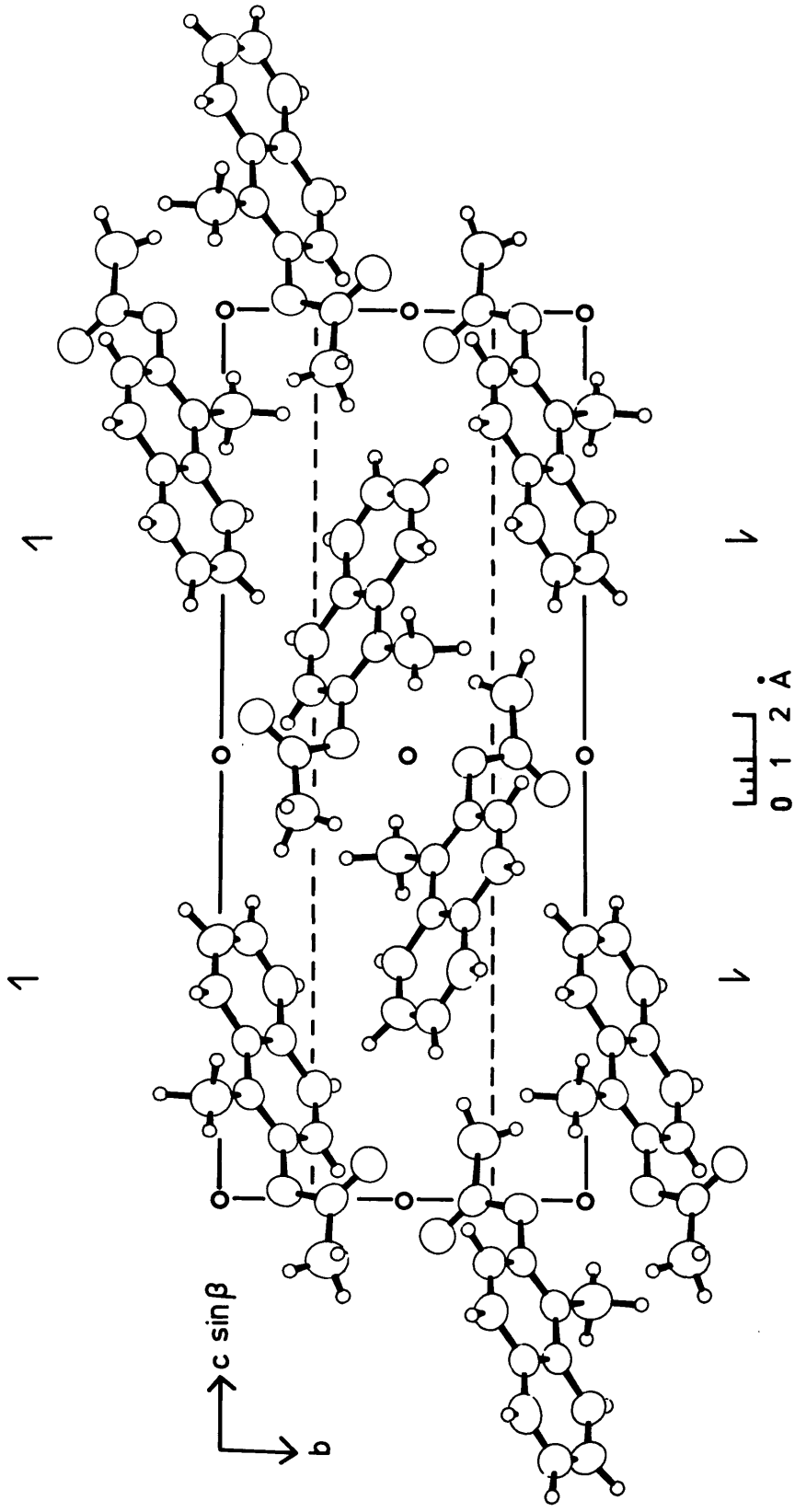

C13
C12
O15
O14
C2
C3
C11
C1
C4
C9
C10
C8
C5
C7
C6

Fig. 3.3 1-Methyl-2-naphthyl acetate: Crystal packing

A view down the a axis


1
1
1
1
c sinβ
b
0 1 2 Å

3.4 1-Isopropyl-2-naphthyl acetate

Experimental

Crystal data

1-isopropyl-2-naphthyl acetate $C_{15}H_{16}O_2$

Unit cell dimensions $\underline{a} = 19.171(5)\ A^{\circ}$

$\underline{b} = 8.591(1)\ A^{\circ}$ $\underline{\alpha}=\underline{\beta}=\underline{\gamma}=90^{\circ}$

$\underline{c} = 15.457(3)\ A^{\circ}$

Space group Pbca (D^{15}_{2h})

$M = 228$ a.m.u.

$V = 2546\ A^{\circ 3}$

$Do = 1.07\ gm.cm^{-3}$

$Dc = 1.190\ gm.cm^{-3}$

$\mu = 0.84\ cm^{-1}$ (Mo-Kα)

$F(000) = 976$

$Z = 8$

The space group was uniquely determined by the systematic absences:

hol when l =2n, hko when h=2n, okl when l=2n.

The crystal used in this analysis was a diamond-shaped plate of dimensions 1x1x0.3 mm.

Data Collection

The cell dimensions were initially obtained from measurements of Weissenberg photographs. These photographs were also used to determine the space group. The crystal was then transferred to the goniometer head of a Hilger and Watts Y290 diffractometer and aligned as described previously. The cell dimensions were redetermined during this procedure and it is these values that are quoted in the crystal data.

The reflexions in the octant hkl were measured in the range $2\theta < 40^{\circ}$ using Mo-Kα radiation. The following scan parameters were employed.

Increment in θ	0.01°
Number of scan steps	80
Time per step	1.5 sec.

Background counts of 30 seconds were taken at each end of the scan range and two strong reflexions were monitored after every 50 intensity measurements. These standard reflexions showed a significant variation towards the end of the data collection and a new set of intensity data had to be obtained using a crystal enclosed in a capillary tube. This crystal appeared to be opaque after a few days but the standards remained reasonably constant.

The measured intensities were placed on a common scale and the integrated intensities (I) yielded 2234 independant structure amplitudes a proportion of which was unobserved.

Reflexions for which $2\theta < 20^{\circ}$ were remeasured using

reduced beam intensity in order to apply a correction for counter saturation.

No correction was made for absorption.

Structure analysis

The phase problem was overcome by using the program MULTAN. The 300 reflexions with the largest values of $|\underline{E}|$ ($|\underline{E}| \geqslant 1.47$) were used to set up triplet relationships. The program selected three reflexions as origin defining and a further three for which the phase was allowed to take on values of 180° or 360° (Table X). These were then used to generate the 8 possible phase sets. The combination producing the highest combined figure of merit gave an $\underline{E}$-map indicating all the non-hydrogen atoms.

A structure factor calculation was carried out using the 1155 independant structure amplitudes for which $|F_o| \geqslant 4\sigma|F_o|$ together with these atomic locations. This gave an initial $\underline{R}$ of 31.3%. On allowing these atoms to vibrate isotropically, a full matrix least squares minimisation converged at $\underline{R}$ = 22.4% after two cycles. The value of $\underline{R}$ fell to 10.0% after two further cycles of full matrix least squares during which anisotropic thermal motion was permitted.

A difference synthesis then revealed most of the hydrogen atoms. Subsequent full matrix least squares (2 cycles) with all the carbon and oxygen atoms

TABLE X SUMMARY OF STRUCTURE DETERMINATION

A. INITIAL SET OF PHASES

REFLECTION				PHASE *	MOD. E
4	1	2	+	360	3.74
2	7	3	+	360	3.23
3	6	9	+	360	2.70
3	8	3		360 OR 180	3.18
5	3	4		360 OR 180	2.95
10	2	2		360 OR 180	2.93

B. STATISTICS

	E1	E2	E3	E4	E5	E6
THEORETICAL FOR CENTRIC	0.798	1.00	0.968	31.73	4.55	0.27
THEORETICAL FOR ACENTRIC	0.886	1.00	0.736	36.79	1.83	0.01
FOUND	0.779	1.00	0.958	32.00	4.60	0.4

* IN DEGREES
\+ ORIGIN DEFINING

MOD. E MODULUS OF E FOR REFLECTION CONCERNED
E1 MEAN VALUE FOR MODULUS OF E
E2 MEAN VALUE FOR MODULUS OF E**2
E3 MEAN VALUE FOR MODULUS OF ((E**2)-1)
E4 % OF REFLECTIONS WITH MODULUS OF E >1.0
E5 % OF REFLECTIONS WITH MODULUS OF E >2.0
E6 % OF REFLECTIONS WITH MODULUS OF E >3.0

(anisotropic motion), these hydrogen positions (isotropic vibration), and also including an allowance for counter saturation reduced R to 8.5% .

The remaining hydrogen coordinates were obtained from a new difference Fourier summation. A weighting scheme of the form:

$$W = 1/(A + BF_o + CF_o^2) \quad \text{with} \quad \begin{array}{l} A = 0.4999 \\ B = -0.3020 \\ C = 0.0049 \end{array}$$

was introduced and two further cycles of full matrix least squares calculations produced a final R of 6.1% .

This structure determination was carried out in collaboration with Dr. P. J. Mallinson (University of Glasgow) who collected the data and solved the structure; the author being responsible for the subsequent refinement.

3.5 Results

Table XI 1-Isopropyl-2-naphthyl acetate: Fractional atomic coordinates

Positional estimated standard deviations are shown in parentheses.

The hydrogen atoms are numbered according to the atoms to which they are attached.

The table shows:

Atom	x	y	z

C(1)	1432(3)	8663(5)	2290(3)
C(2)	0908(3)	8983(6)	1715(3)
C(3)	0469(3)	10296(6)	1763(3)
C(4)	0562(3)	11325(6)	2412(4)
C(5)	1163(3)	12127(6)	3755(4)
C(6)	1646(3)	11869(7)	4372(3)
C(7)	2088(3)	10589(7)	4314(4)
C(8)	2029(3)	9574(6)	3648(3)
C(9)	1518(3)	9745(6)	2988(3)
C(10)	1083(3)	11088(6)	3049(3)
C(11)	1879(2)	7193(6)	2222(3)
C(12)	0740(3)	8276(7)	0231(3)
C(13)	0470(3)	6950(7)	-0301(3)
C(17)	1455(4)	5729(7)	2396(5)
C(18)	2274(3)	7090(7)	1374(4)
O(14)	0744(2)	7858(4)	1083(2)
O(15)	0929(2)	9496(5)	-0026(3)
H(3)	0114(26)	10370(61)	1253(32)
H(4)	0266(24)	12342(61)	2424(31)
H(5)	0855(23)	13030(53)	3719(30)
H(6)	1686(24)	12616(61)	4874(29)
H(7)	2421(24)	10459(51)	4729(26)
H(8)	2325(20)	8747(49)	3601(25)
H(11)	2265(27)	7276(65)	2686(33)
H(131)	0534(37)	7043(92)	-0963(48)
H(132)	-0024(31)	6946(66)	-0308(36)
H(133)	0670(41)	6045(79)	-0150(48)
H(171)	1750(26)	4924(58)	2401(33)
H(172)	1229(38)	5782(88)	2949(54)
H(173)	1067(33)	5577(76)	1932(42)
H(181)	2663(26)	6283(64)	1419(31)
H(182)	2494(28)	7935(62)	1210(34)
H(183)	1936(42)	6796(84)	0877(44)

Table XII 1-Isopropyl-2-naphthyl acetate: Thermal parameters

Carbon and oxygen values are anisotropic.

Hydrogen values are isotropic.

Estimated errors in the last digit are shown in parentheses.

All figures are multiplied by 10^3.

The anisotropic temperature factor expression used was of the form described by equation (12) in chapter one, the coefficients being in terms of the mean square amplitudes of vibration U_{ij} .

The table shows:

Atom	U_{11} or U	U_{22}	U_{33}	U_{13}	U_{12}	U_{23}

C(1)	49(3)	43(3)	44(3)	4(3)	8(3)	8(2)
C(2)	49(3)	40(3)	46(3)	-5(3)	3(3)	3(3)
C(3)	51(3)	55(3)	53(3)	14(3)	-1(3)	3(3)
C(4)	57(3)	45(3)	64(4)	19(3)	3(3)	6(3)
C(5)	64(4)	46(3)	64(4)	-1(3)	18(3)	2(3)
C(6)	72(4)	59(4)	53(3)	-12(3)	2(3)	-6(3)
C(7)	63(4)	64(4)	57(4)	-8(3)	-10(3)	1(3)
C(8)	47(3)	48(3)	60(3)	5(3)	1(3)	5(3)
C(9)	43(3)	51(3)	44(3)	-1(3)	8(2)	11(2)
C(10)	49(3)	39(3)	54(3)	2(3)	8(3)	8(3)
C(11)	50(3)	45(3)	54(3)	9(3)	7(3)	8(3)
C(12)	57(3)	56(4)	53(4)	5(3)	-3(3)	5(3)
C(13)	75(4)	67(4)	58(3)	11(3)	-9(3)	-12(3)
C(17)	78(4)	51(4)	118(6)	14(3)	17(4)	30(4)
C(18)	71(4)	57(4)	68(4)	19(3)	21(3)	8(3)
O(14)	59(2)	43(2)	51(2)	-3(2)	-4(2)	6(2)
O(15)	127(4)	66(3)	59(2)	-22(3)	3(3)	16(2)
H(3)	70(16)					
H(4)	62(15)					
H(5)	52(14)					
H(6)	59(15)					
H(7)	47(14)					
H(8)	33(12)					
H(11)	78(18)					
H(131)	136(29)					
H(132)	87(19)					
H(133)	130(28)					
H(171)	63(16)					
H(172)	152(30)					
H(173)	108(22)					
H(181)	63(16)					
H(182)	75(17)					
H(183)	138(28)					

TABLE XIII

1-ISOPROPYL-2-NAPHTHYL ACETATE:
INTRAMOLECULAR BONDED DISTANCES(ANGSTROMS)
STANDARD DEVIATIONS (ANGSTROMS) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	DIST.	ATOM1	ATOM2	DIST.
C1	C2	1.371(7)	C12	O15	1.179(7)
C1	C9	1.431(7)	C3	H3	1.041(53)
C1	C11	1.524(7)	C4	H4	1.033(53)
C2	C3	1.408(7)	C5	H5	0.976(47)
C2	O14	1.414(6)	C6	H6	1.017(51)
C3	C4	1.348(8)	C7	H7	0.910(46)
C4	C10	1.412(8)	C8	H8	0.920(43)
C5	C6	1.351(8)	C11	H11	1.052(55)
C5	C10	1.420(8)	C13	H131	1.046(77)
C6	C7	1.390(9)	C13	H132	0.933(64)
C7	C8	1.353(8)	C13	H133	0.942(75)
C8	C9	1.428(7)	C17	H171	0.892(53)
C9	C10	1.430(7)	C17	H172	0.977(88)
C11	C17	1.522(8)	C17	H173	1.038(69)
C11	C18	1.518(8)	C18	H181	1.023(55)
C12	C13	1.492(8)	C18	H182	0.891(56)
C12	O14	1.367(6)	C18	H183	1.042(80)

TABLE XIV 1-ISOPROPYL-2-NAPHTHYL ACETATE: SOME INTRAMOLECULAR NON-BONDED SEPARATIONS

ATOM1	ATOM2	DIST #	ATOM1	ATOM2	DIST #
C(1)	C(8)	2.516	O(15)	H(3)	2.63
C(11)	O(14)	2.855	O(15)	H(183)	3.32
C(11)	H(8)	2.657	H(4)	H(5)	2.37
O(14)	C(17)	3.053	H(7)	H(8)	2.29
O(14)	C(18)	3.039	H(8)	H(11)	1.90

IN ANGSTROMS

TABLE XV 1-ISOPROPYL-2-NAPHTHYL ACETATE: INTERMOLECULAR CONTACTS OF LESS THAN 4.0 ANGSTROMS

ATOM1	ATOM2		DIST #	ATOM1	ATOM2		DIST #
C(5)	C(17)	*	3.782	C(4)	C(17)	****	3.910
C(13)	C(13)	**	3.917	C(4)	O(14)	****	3.662
C(6)	C(8)	***	3.619	C(5)	C(13)	****	3.940
C(7)	C(8)	***	3.955	C(5)	O(14)	****	3.718
C(8)	C(11)	***	3.783	C(7)	C(13)	*****	3.839
C(8)	C(17)	***	3.630	C(7)	C(18)	*****	3.945
C(9)	C(11)	***	3.908	C(8)	C(13)	*****	3.645
C(9)	C(18)	***	3.956	C(9)	C(13)	*****	3.627
C(3)	C(17)	****	3.927	C(10)	C(13)	*****	3.834
C(4)	C(2)	****	3.869				

IN ANGSTROMS

THE ASTERISKS(*) REFER TO THE FOLLOWING TRANSFORMATIONS OF THE ATOMIC COORDINATES

*	X,	1.0+Y,	Z
**	-X,	1.0-Y,	-Z
***	0.5-X,	0.5+Y,	Z
****	-X,	0.5+Y,	0.5-Z
*****	X,	1.5-Y,	0.5+Z

TABLE XVI

1-ISOPROPYL-2-NAPHTHYL ACETATE: VALENCY ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ANGLE	ATOM1	ATOM2	ATOM3	ANGLE
C9	C1	C2	115.7(4)	C11	C1	C2	122.2(4)
C11	C1	C9	122.1(4)	O14	C2	C1	118.2(4)
C3	C2	C1	124.7(5)	O14	C2	C3	116.8(4)
C4	C3	C2	119.0(5)	C10	C4	C3	121.1(5)
C10	C5	C6	121.0(5)	C7	C6	C5	120.2(5)
C8	C7	C6	120.7(5)	C9	C8	C7	122.4(5)
C10	C9	C1	120.9(4)	C8	C9	C1	123.2(5)
C10	C9	C8	115.9(4)	C5	C10	C4	121.6(5)
C9	C10	C4	118.6(4)	C9	C10	C5	119.8(5)
C18	C11	C1	112.9(4)	C17	C11	C1	111.7(4)
C18	C11	C17	112.2(5)	O14	C12	C13	109.5(4)
O15	C12	C13	127.0(5)	O15	C12	O14	123.4(5)
C12	O14	C2	119.7(4)	H3	C3	C2	113.8(31)
H3	C3	C4	127.2(31)	H4	C4	C3	119.3(28)
H4	C4	C10	119.4(28)	H5	C5	C6	126.0(28)
H5	C5	C10	112.9(28)	H6	C6	C5	119.7(29)
H6	C6	C7	120.1(29)	H7	C7	C6	118.0(29)
H7	C7	C8	121.3(29)	H8	C8	C7	121.8(26)
H8	C8	C9	115.8(26)	H11	C11	C1	107.1(32)
H11	C11	C17	108.4(31)	H11	C11	C18	104.0(30)
H131	C13	C12	115.9(44)	H132	C13	C12	110.0(37)
H133	C13	C12	111.9(47)	H132	C13	H131	96.5(54)
H133	C13	H131	104.3(64)	H133	C13	H132	117.6(62)
H172	C17	C11	111.8(47)	H173	C17	C11	111.0(38)
H171	C17	C11	106.7(34)	H172	C17	H171	107.7(59)

VALENCY ANGLES (CONTINUED)

ATOM1	ATOM2	ATOM3	ANGLE	ATOM1	ATOM2	ATOM3	ANGLE
H173	C17	H171	110.0(51)	H173	C17	H172	109.6(60)
H181	C18	C11	109.7(29)	H182	C18	C11	115.1(36)
H183	C18	C11	107.8(45)	H182	C18	H181	104.8(47)
H183	C18	H181	110.5(54)	H183	C18	H182	109.0(56)

TABLE XVII

1-ISOPROPYL-2-NAPHTHYL ACETATE: TORSION ANGLES(DEGREES)
STANDARD DEVIATIONS(DEGREES) ARE SHOWN IN PARENTHESES

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
C9	C1	C2	C3	1.7(8)	C9	C1	C2	O14	-172.1(4)
C11	C1	C2	C3	178.3(5)	C11	C1	C2	O14	4.5(7)
C2	C1	C9	C8	178.8(5)	C2	C1	C9	C10	-1.8(7)
C11	C1	C9	C8	2.1(8)	C11	C1	C9	C10	-178.4(4)
C2	C1	C11	C17	-67.0(7)	C2	C1	C11	C18	60.5(7)
C9	C1	C11	C17	109.4(6)	C9	C1	C11	C18	-123.1(5)
C1	C2	C3	C4	-0.4(8)	O14	C2	C3	C4	173.5(5)
C1	C2	O14	C12	-125.9(5)	C3	C2	O14	C12	59.9(6)
C2	C3	C4	C10	-0.9(8)	C3	C4	C10	C5	-177.0(5)
C3	C4	C10	C9	0.7(8)	C10	C5	C6	C7	1.5(9)
C6	C5	C10	C4	178.0(5)	C6	C5	C10	C9	0.3(8)
C5	C6	C7	C8	-1.5(9)	C6	C7	C8	C9	-0.4(9)
C7	C8	C9	C1	-178.4(5)	C7	C8	C9	C10	2.1(8)
C1	C9	C10	C4	0.7(8)	C1	C9	C10	C5	178.5(5)
C8	C9	C10	C4	-179.9(5)	C8	C9	C10	C5	-2.0(7)
C13	C12	O14	C2	-173.4(4)	O15	C12	O14	C2	7.6(8)
C2	C1	C11	H11	174.3(32)	C9	C1	C11	H11	-9.2(32)
C1	C2	C3	H3	177.3(33)	O14	C2	C3	H3	-8.9(33)
C2	C3	C4	H4	174.6(33)	H3	C3	C4	C10	-178.2(38)
H3	C3	C4	H4	-2.6(50)	H4	C4	C10	C5	7.4(34)
H4	C4	C10	C9	-174.8(33)	C10	C5	C6	H6	-179.5(33)
H5	C5	C6	C7	-174.8(35)	H5	C5	C6	H6	4.2(48)
H5	C5	C10	C4	-5.2(31)	H5	C5	C10	C9	177.0(30)
C5	C6	C7	H7	177.6(33)	H6	C6	C7	C8	179.5(33)
H6	C6	C7	H7	-1.3(47)	C6	C7	C8	H8	177.6(31)

TORSION ANGLES (CONTINUED)

ATOM1	ATOM2	ATOM3	ATOM4	ANGLE	ATOM1	ATOM2	ATOM3	ATOM4	ANGLE
H7	C7	C8	C9	-179.5(34)	H7	C7	C8	H8	-1.5(47)
H8	C8	C9	C1	3.5(30)	H8	C8	C9	C10	-176.0(29)
C1	C11	C17	H171	-174.1(36)	C1	C11	C17	H172	-56.6(52)
C1	C11	C17	H173	66.1(41)	C18	C11	C17	H171	58.0(36)
C18	C11	C17	H172	175.6(52)	C18	C11	C17	H173	-61.8(41)
H11	C11	C17	H171	-56.2(48)	H11	C11	C17	H172	61.3(62)
H11	C11	C17	H173	-176.0(52)	C1	C11	C18	H181	164.6(32)
C1	C11	C18	H182	46.8(40)	C1	C11	C18	H183	-75.1(46)
C17	C11	C18	H181	-68.1(32)	C17	C11	C18	H182	174.1(40)
C17	C11	C18	H183	52.2(46)	H11	C11	C18	H181	48.8(45)
H11	C11	C18	H182	-69.0(51)	H11	C11	C18	H183	169.2(56)
O14	C12	C13	H131	-167.3(47)	O14	C12	C13	H132	84.7(40)
O14	C12	C13	H133	-47.9(51)	O15	C12	C13	H131	11.6(47)
O15	C12	C13	H132	-96.4(41)	O15	C12	C13	H133	131.0(51)

THE ANGLE 1-2-3-4 IS DEFINED AS POSITIVE IF, WHEN VIEWED ALONG THE 2-3 BOND, ATOM 1 HAS TO BE ROTATED CLOCKWISE TO ECLIPSE ATOM 4

TABLE XVIII 1-ISOPROPYL-2-NAPHTHYL ACETATE: MEAN PLANES CALCULATIONS

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
1.	C(1)		-0.002(5)
	C(2)		0.024(5)
	C(3)		0.017(5)
	C(4)		-0.019(5)
	C(5)		-0.002(5)
	C(6)		0.030(6)
	C(7)		0.010(6)
	C(8)		-0.017(5)
	C(9)		-0.013(5)
	C(10)		-0.026(5)
		C(11)	0.049(5)
		O(14)	0.205(3)
		H(4)	-0.102(49)
		H(5)	-0.058(45)
		H(8)	-0.051(39)

TABLE XVIII (CONTINUED)

	ATOMS IN PLANE	ATOMS OUT OF PLANE	DEVIATION (ANGSTROMS)
2.	C(12)		0.000(5)
	C(13)		0.000(6)
	O(14)		0.000(3)
		O(15)	-0.013(5)

THE OUT OF PLANE ATOMS WERE NOT INCLUDED IN THE DERIVATION OF THE PLANES.

THE EQUATIONS OF THESE PLANES ARE:

1. $-0.6516X - 0.5278Y + 0.5448Z = -3.7867$
2. $-0.9315X + 0.3493Y + 0.1015Z = 1.1986$

Fig. 3.4 1-Isopropyl-2-naphthyl acetate: A view of the molecule

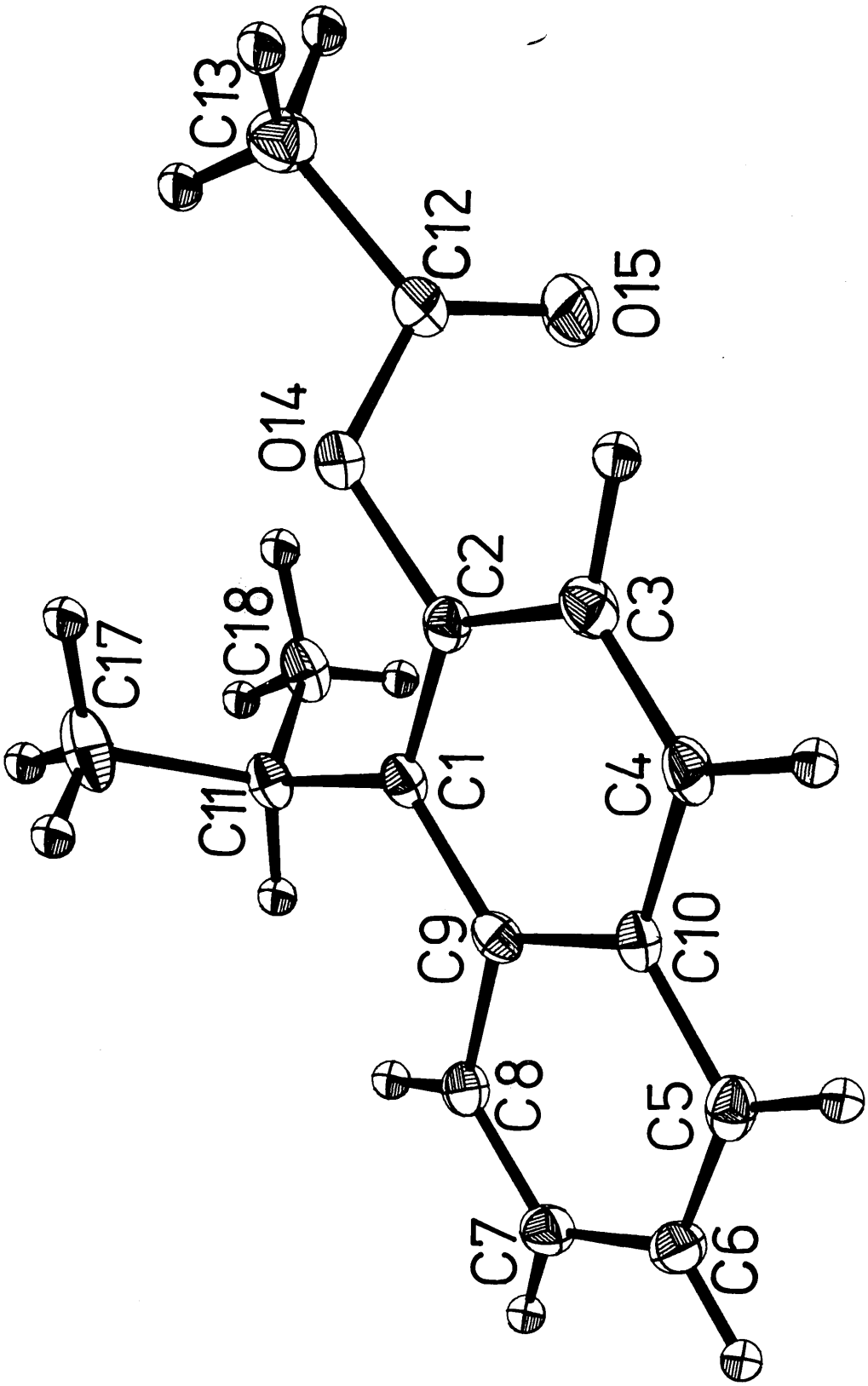
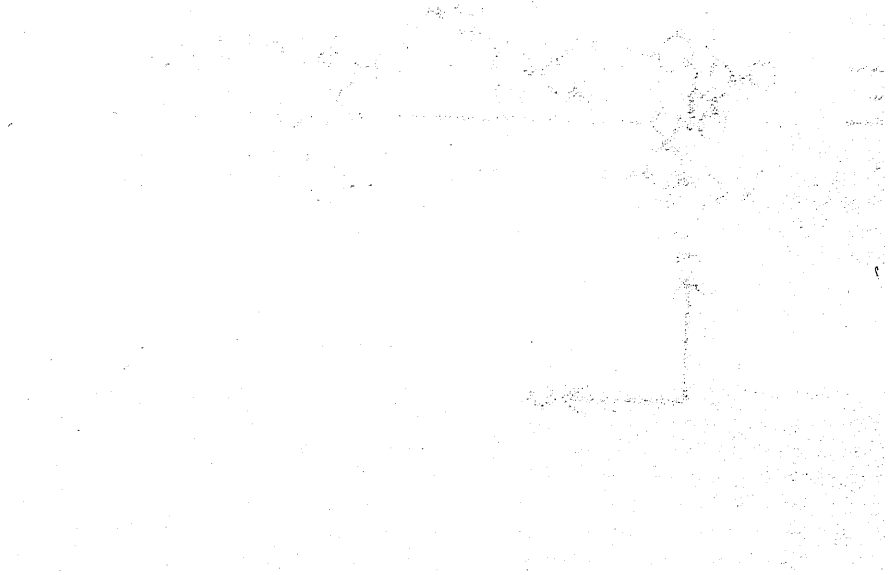
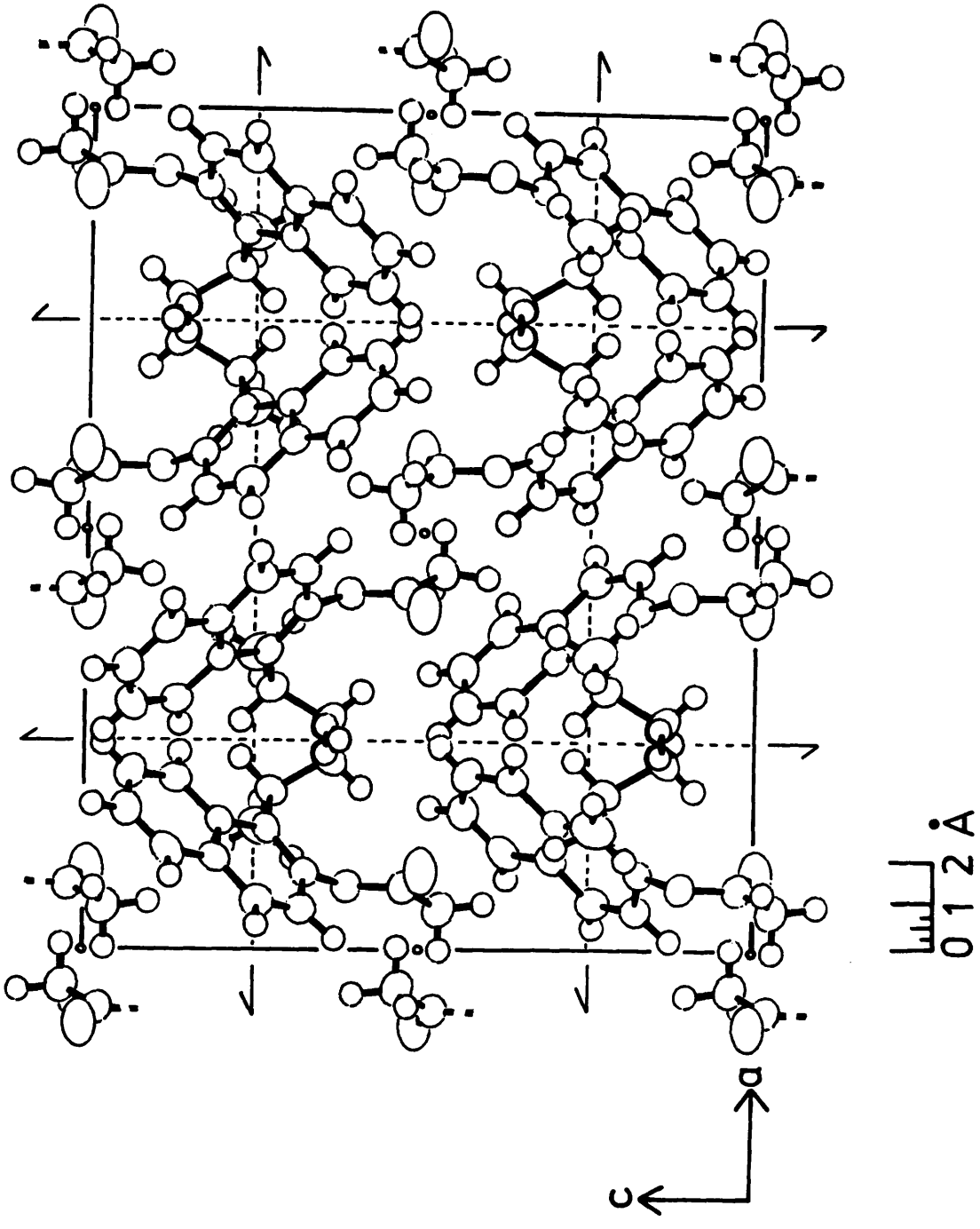

C13
C12
O15
O14
C2
C3
C18
C17
C1
C11
C4
C9
C10
C8
C5
C7
C6

Fig. 3.5 1-Isopropyl-2-naphthyl acetate: Crystal packing

A view down the b axis




a
c
0 1 2 Å

3.6 Discussion of results

Tables II - IX and XI - XVIII summarise the results of the analyses for the methyl- and isopropyl-derivatives of 2-naphthyl acetate respectively. Figures 3.2 and 3.4 illustrate views of the respective molecules and Fig. 3.3 shows the crystal packing of 1-methyl-2-naphthyl acetate viewed along the a axis while Fig. 3.5 is a drawing of the crystal packing of its isopropyl homologue viewed along the b axis.

The final and observed structure factors are listed in Tables XX and XXI respectively.

The analysis shows that the geometry of the methyl compound is very similar to that observed in naphthalene (3)

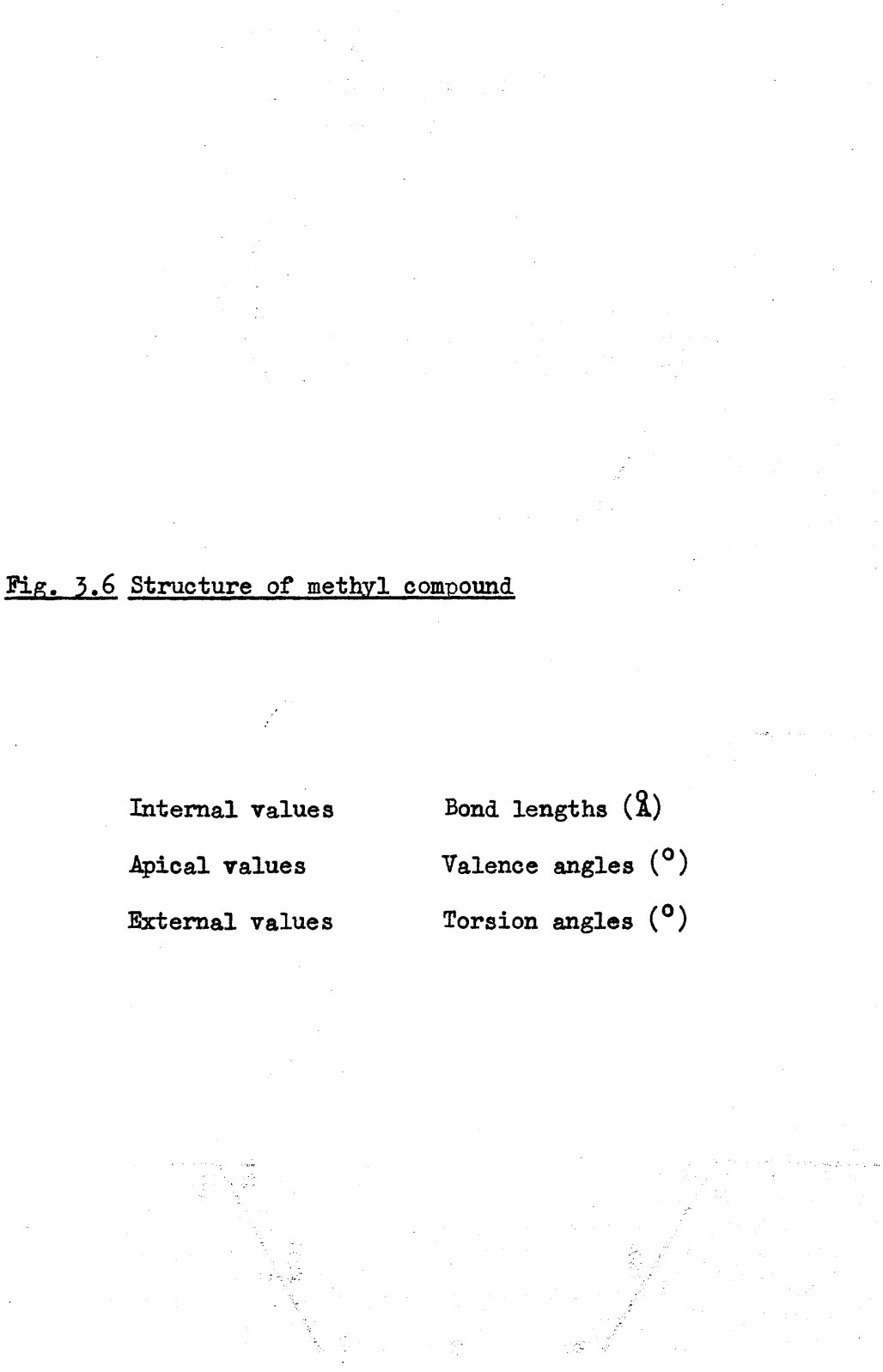


Fig. 3.6 Structure of methyl compound

Internal values	Bond lengths (Å)
Apical values	Valence angles (°)
External values	Torsion angles (°)

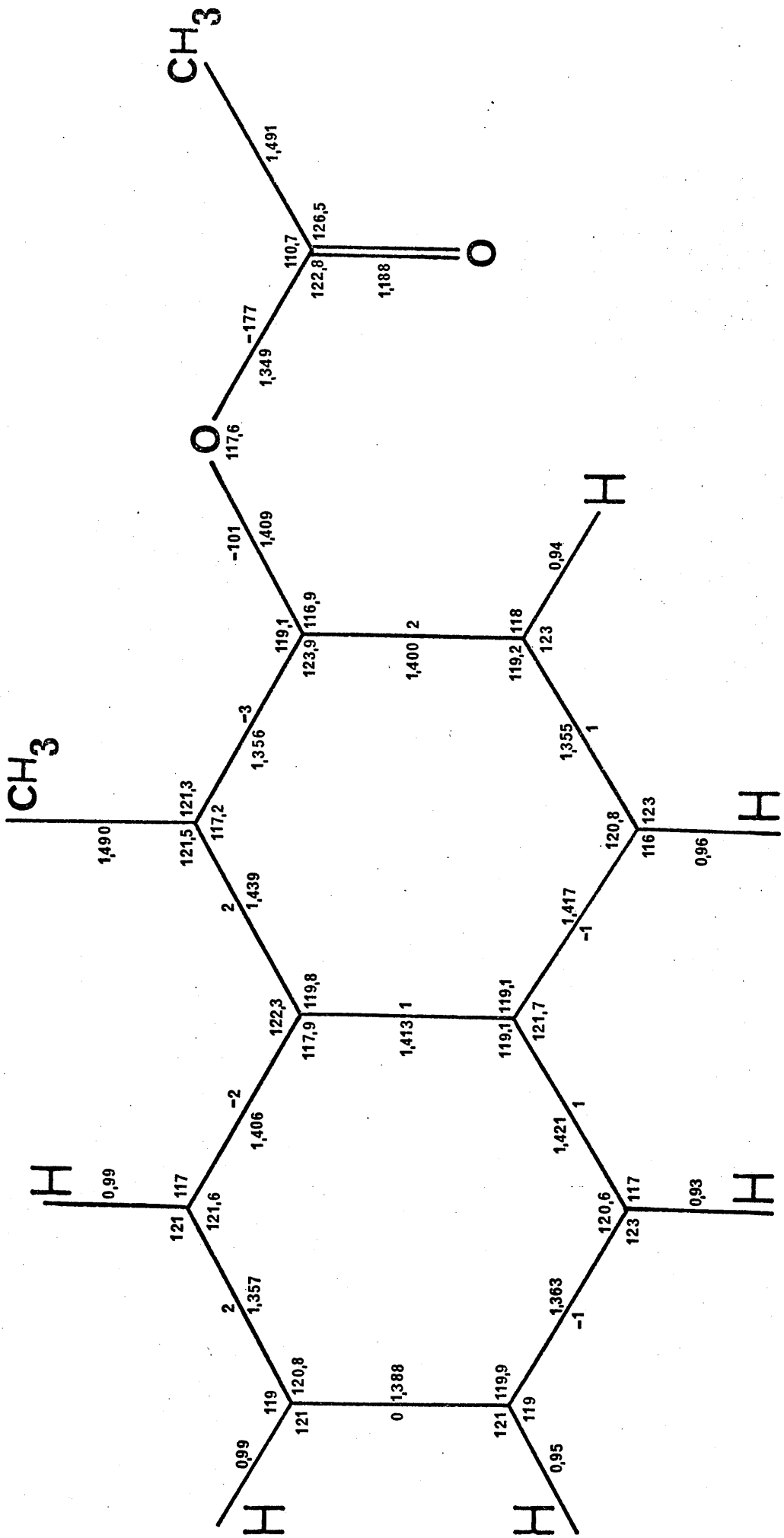
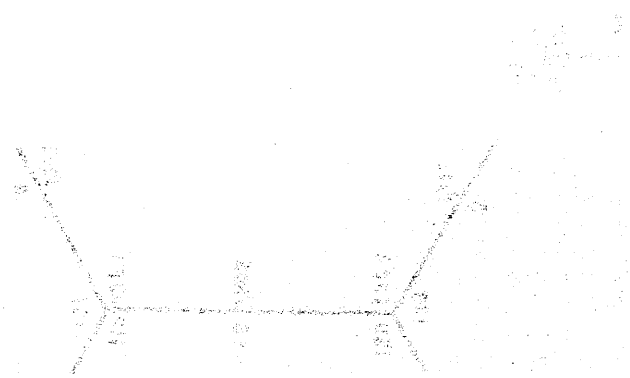
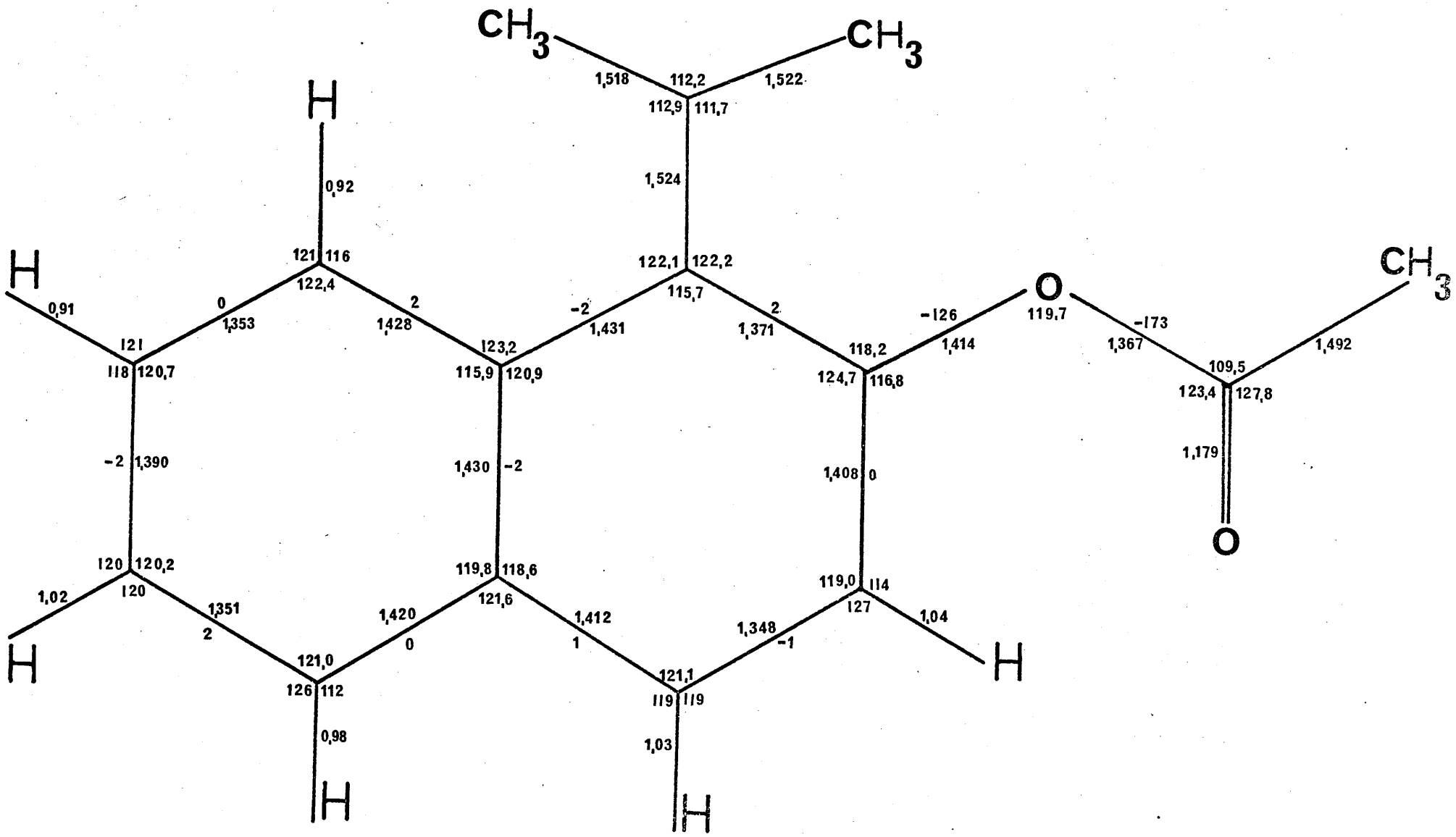

CH3
1,491
126,5
110,7
122,8
1,188
O
-177
1,349
O
117,6
-101
1,409
H
0,94
119,1
116,9
123,9
2
1,400
119,2
118
123
-3
1,356
1,355
1
CH3
1,490
121,5
121,3
117,2
2
1,439
120,8
123
116
H
0,96
-2
1,406
1,417
-1
122,3
119,8
117,9
1
1,413
119,1
119,1
121,7
121
117
121,6
0,99
H
2
1,357
1,421
1
120,6
117
123
H
0,93
119
120,8
121
0
1,388
119,9
121
119
-1
1,363
0,99
H
0,95
H

Fig. 3.7 Structure of isopropyl compound

Internal values	Bond lengths (Å)
Apical values	Valence angles (°)
External values	Torsion angles (°)




CH3
CH3
1,518
112,2
1,522
112,9
111,7
H
0,92
1,524
H
0,91
121
116
122,1
122,2
O
CH3
122,4
115,7
119,7
-126
-173
0
2
-2
2
1,353
1,428
1,431
1,371
1,414
1,367
1,492
121
123,2
118,2
109,5
118
120,7
115,9
120,9
124,7
116,8
123,4
127,8
-2
1,390
1,430
-2
1,408
0
1,179
O
120
120,2
119,8
118,6
119,0
114
1,02
120
121,6
127
1,04
1,351
1,420
1,412
1,348
2
0
1
-1
H
H
121,0
121,1
126
112
119
119
0,98
1,03
H
H

indicating that very little additional strain has been imposed by the 1, 2- substituents. The naphthalene nucleus is essentially planar since the maximum ring torsion angle ($\underline{\omega}$) is -3° with $\Sigma|\underline{\omega}| = 16^{\circ}$ and $\Sigma\,\underline{\omega} = 2$. The largest displacement from the mean plane of the ring is $0.03A^{\circ}$ at C(2).(Table IX). This is not entirely unexpected because previous work has shown that peri-strain is usually minimized by out of plane bending and in-plane splaying of the 1, 8- substituents and that the naphthalene system is only distorted in extreme cases. Thus, 1, 8- dimethyl-naphthalene (4) and 1, 8- diphenyl-naphthalene (5) have planar aromatic systems, while 1, 8-di(bromomethyl)-naphthalene (6); 1, 4, 5, 8, -tetrachlor-onaphthalene (7) and 1, 4, 5, 8- tetraphenyl-naphthalene (8) all exhibit deformation of the naphthalene nucleus.

Any peri -strain present in 1- methyl-2-naphthyl acetate must therefore manifest itself by causing either out of plane or in-plane deformations. The out of plane bending of C(11) and H(8) is minimal as the displacements of these atoms from the mean plane of the naphthalene ring (-0.071 and $0.02A^{\circ}$ respectively) are barely significant although they may be in the opposite sense. Likewise, the C(11) - C(1) - C(9) - C(8) torsion angle of 3°, the C(1) -C(9) - C(8) - H(8) value of 2° and the angle between the planes defined by C(1) - C(8) - H(8) and C(8) - C(1) - C(11) , (4°) , hardly provide reasonable evidence of out of plane bending.

The evidence for in-plane splaying is more satisfactory. The C(1) - C(9) - C(8) valence angle opens up to 122.3°, which is over twenty standard deviations

greater than the "equilibrium" value of 120°, and 1.0° larger than that observed in unsubstituted naphthalene (3). The C(9) - C(1) - C(11) angle is 121.5° and this also indicates some in-plane deformation. There is a fairly large estimated standard deviation (1.5°) on the H(8) - C(8) - C(9) value of 117° so that it is difficult to assess the distortion at C(8) from this measurement. However, the C(1) .... C(8) intramolecular non-bonded distance of 2.494A° is a little longer than the C(4).... C(5) separation (2.481A°) and this difference is just large enough to indicate the necessity for some relief of strain at C(1), C(8), but comparison with the geometry in this region in 1, 8 disubstituted naphthalenes (e.g. 4, 6) shows the relatively small amount of strain present in 1- methyl - 2 - naphthylacetate.

There are also variations in the naphthalene nucleus H-C-C bond angles but these angles have standard deviations which are too large for them to be used to investigate the possible transmission of peri-strain aroung the ring as reported by Bright et al (4) but the H(4).....H(5) separation of 2.39A° is reasonably correct and not shortened to c.2.2A° as in 1, 8 dimethyl naphthalene so that this transmission effect is not observed.

The previous discussion shows that 1-methyl-2-naphthyl acetate is far less strained than the 1, 8 disubstituted naphthalenes for which results are available. The rate measurements on the autoxidation of alkyl naphthols by Brady and Carnduff (2) suggest that the

replacement of the methyl substituent at C(1) by an isopropyl function should cause a substantial increase in peri-strain.

The present study does not support this suggestion. A comparison of the pertinent geometrical parameters for the two compounds is given in Table XIX. In general the increase in strain in going from C(1)-methyl to C(1)-isopropyl is not as large as might be anticipated from the rate measurements.

Thus the relative values for the torsion angles and out of plane displacements in the naphthalene nucleus are unchanged within the limits of this experiment as are the displacements of C(11) and C(8) from the mean plane of the aromatic system.

Out of plane deformation of C(11) and H(8) is not increased in the isopropyl homologue since neither the displacement of these atoms from the mean plane of the naphthalene ring nor the C(11) - C(1) - C(9) - C(8) and C(1) - C(9) - C(8) - H(8) torsion angles show any significant variation. The angle between the planes defined by C(11), C(2), C(8) and H(8), C(8), C(1) remains at 4^{o}.

In-plane bending at C(1) and C(8) is again the only type of distortion which is large enough to be significant.

The isopropyl substitution for methyl at C(1) opens the C(11) - C(1) - C(9) angle by a further 0.6^{o} to 122.1^{o} and the C(1) - C(9) - C(8) value increases by almost 1^{o}

TABLE XIX COMPARISON OF PERI-STRAIN IN METHYL AND ISOPROPYL DERIVATIVES

PARAMETER	METHYL	ISOPROPYL
MAX. TORSION ANGLE IN NAPHTHALENE NUCLEUS *	3	2
OMEGA	2	0
MOD. OMEGA	16	14
MAX. DISPLACEMENT OF RING CARBON ATOMS ++	0.03 AT C(2)	0.03 AT C(6)
MAX. DISPLACEMENT OF		
C(11) ++	-0.07	0.05
H(8) ++	0.02	-0.05
NON-BONDED DISTANCES +		
C(1)....C(8)	2.494	2.516
C(4)....C(5)	2.481	2.472
O(15)....H(3)	3.18	2.63
H(4)...H(5)	2.39	2.37
VALENCE ANGLES *		
C(9)-C(1)-C(11)	121.5	122.1
C(1)-C(9)-C(8)	122.3	123.2
C(4)-C(10)-C(5)	121.8	121.6
C(9)-C(8)-H(8)	117	116
TORSION ANGLES *		
C(11)-C(1)-C(9)-C(8)	3	2
C(1)-C(2)-O(14)-C(12)	-101	-126
C(1)-C(9)-C(8)-H(8)	2	4
"C(11)-C(1)-C(8)-H(8)"	4	4

SYMBOLS EXPLAINED ON FOLLOWING PAGE

EXPLANATION OF SYMBOLS IN TABLE XIX

*	IN DEGREES
+	IN ANGSTROMS
OMEGA	THE SUM OF THE TORSION ANGLES OF THE NAPHTHALENE NUCLEUS
MOD. OMEGA	THE SUM OF THE MODULII OF THE TORSION ANGLES OF THE NAPHTHALENE NUCLEUS
++	FROM MEAN PLANE THROUGH NAPHTHALENE NUCLEUS(ANGSTROMS)

to 123.2°. Similar enlargement of the latter angle has also been observed in 1.8-dimethyl-naphthalene (4) (125.2°) and in 1,8-di(bromomethyl)-naphthalene (6) (127°) so there is clearly a progression in the distortion of C(1) - C(9) - C(8) from 122.3° (1-methyl) to 127° (1,8-di(bromomethyl)).

This deformation increases the C(1) ..... C(8) separation throughout the series. The relevant values being 2.494A° (methyl), 2.516A°(isopropyl), 2.543 (1,8-dimethyl), and 2.57 (1,8-di(bromomethyl)).

1-Isopropyl-2-naphthyl acetate shows no evidence for transmission of the peri-strain to the C(4), C(5) locations since neither the C(4) .....C(5) nor H(4) ..... H(5) distances (2.472A° and 2.37A° respectively) are decreased by substantial amounts.

In the isopropyl derivative the C(11) substituents are arranged so that H(11) almost eclipses the C(1) - C(9) bond (C(9) - C(1) - C(11) - H(11) torsion angle is -9°) this is in contrast to the situation in the methyl compound where one of the C(11) hydrogens is located so as to give a C(2) - C(1) - C(11) - H(112) torsion angle of 2°. H(11) appears to be separated from H(8) by 1.90A° (Table XIV) but the estimated standard deviations of the fractional co-ordinates of these atoms are in the range 0.002 to 0.006A° and the C(8) - H(8) bond length is found as 0.92A° (Table XIII) so that this non-bonded distance is probably not significant.

Further evidence of a difference in strain in these two 1-alkyl-2-naphthyl acetates is provided by the conformation adopted by the acetate side chain. In the methyl derivative the ester function rotates with respect to the naphthalene nucleus to give a C(1) - C(2) - O(14) - C(12) torsion angle of -101°. The reason for this is to reduce the H(3) ..... O(15) non-bonded interaction by increasing the separation of these two atoms to $3.18A^{\circ}$. In the isopropyl compound the replacement of two of the C(11) hydrogens by methyl functions restricts the amount of torsional rotation in the acetate group and the C(1) - C(2) -O(14) - C(12) torsion angle is then -126°. This is only sufficient to separate H(3) and O(15) by $2.63A^{\circ}$.

The results from the x-ray analysis of these two derivatives of 2-naphthol do not confirm the hypothesis of Brady and Carnduff regarding steric strain in 1-alkyl-2-naphthols. Subsequent crystal analysis on other compounds with different substituents at R1, R2 and R3 (Fig. 3.1) when compared with this study may allow an interpretation of the observed rates of autoxidation.

Table XX 1-Methyl-2-naphthyl acetate: Final structure factors

The table shows:

L* $|F_o|$ $|F_c|$ Phase(°)

* Reflections sorted into groups with common H,K indices (shown in each group heading)

7,4,L

0	13	8
-1	30	28
-2	23	23
-3	12	-9
-4	39	-37
-5	11	-11
-7	13	11

7,3,L

6	16	-13
4	13	-11
0	13	16
-1	32	30
-2	22	-18
-3	35	-36
-4	44	-41
-6	16	16
-8	31	25
-9	17	17

7,2,L

8	11	-6
6	12	-6
5	11	6
4	12	-11
3	16	-15
1	10	10
-1	13	6
-2	17	-19
-3	44	-43
-4	27	-26
-5	12	9
-6	15	16
-8	22	-20
-9	12	12

7,1,L

5	19	-19
3	11	-9
2	23	-21
1	15	14
0	11	14
-3	24	-23
-4	34	33
-5	14	13
-6	13	17
-7	10	-6
-8	14	14
-12	12	9

7,0,L

8	21	18
4	30	-26
2	36	31
0	40	38
-2	30	25
-4	37	29
-6	14	8
-8	31	27
-10	13	11
-12	15	-11

6,6,L

7	16	13
4	23	17
3	11	1
1	14	12
0	14	-11
-6	10	-8
-8	20	-17

6,5,L

10	12	-8
7	28	-29
6	27	28
5	12	9
4	15	-10
1	14	-10
-1	34	-32
-2	17	16
-3	17	-16
-9	17	-17
-10	40	35
-11	18	21

6,4,L

9	32	-30
7	11	2
6	29	31
4	10	3
3	11	-8
1	14	-16
0	30	30
-1	11	0
-2	20	-21
-4	28	25
-5	17	18
-7	17	-17
-9	18	-14
-11	33	30
-13	28	-26

6,3,L

13	28	24
12	25	23
10	17	13
8	27	23
7	27	30
6	31	29
5	16	13
3	20	-19
2	17	18
1	13	-8
0	37	-37
-1	22	24
-2	31	-29
-3	29	27
-4	47	46
-5	57	54
-7	11	-13
-9	13	14
-10	17	15
-11	11	12
-12	15	12
-14	15	11

6,2,L

14	23	21
13	34	31
12	13	7
11	14	-13
9	11	-11
6	16	14
5	13	-15
3	13	13
2	37	-36
1	27	31
0	10	-8
-2	16	17
-3	57	54
-4	84	80
-5	26	24
-6	48	-49
-7	32	-32
-9	16	10
-10	11	6
-13	19	-19
-16	26	-24

6,1,L

14	23	23
11	63	-59
10	51	-47
9	14	14
8	17	-13
7	10	8
6	14	-15
5	21	24
4	24	-21
1	30	-28
-2	13	-17
-3	55	51
-5	94	-89
-6	134	-130
-7	15	-15
-8	44	-43
-9	30	-30
-10	24	-24
-11	18	21
-15	23	-17

6,0,L

14	41	41
12	66	-65
10	23	-18
8	10	10
6	13	9
4	19	-11
2	41	-40
0	28	-31
-2	17	20
-6	85	-83
-8	80	83
-10	16	17
-12	19	21
-14	13	12
-16	38	-33

5,8,L

0	13	-9
-1	11	-12

5,7,L

7	14	14
5	19	-15
4	23	21
3	13	-12
1	16	-18
0	33	-31
-2	15	15
-4	28	28
-5	15	-17
-8	16	20

5,6,L

9	14	17
6	12	12
3	10	6
0	12	-14
-1	23	26
-2	74	79
-3	18	18
-5	32	31
-6	14	11
-11	17	-15
-12	23	-21

5,5,L

14	11	-9
13	16	15
12	14	-11
11	34	34
9	24	23
8	15	16
7	45	45
6	13	12
5	17	19

5,5,L

4	11	-16
3	29	31
2	11	-10
0	17	21
-1	12	10
-2	11	-5
-3	12	17
-4	47	-50
-6	17	-17
-7	16	11
-8	11	-11
-9	17	16
-11	21	19
-12	32	-30
-14	12	10
-15	18	19

5,4,L

15	22	19
14	15	-11
12	10	-2
10	21	-19
9	14	-8
7	19	-20
6	52	-53
5	43	-48
4	24	-21
3	11	-14
2	15	18
1	33	-32
0	14	-16
-1	32	36
-3	55	-59
-5	25	-28
-6	27	24
-7	25	-28
-9	13	-11
-10	14	-16
-12	40	-42
-14	19	20
-15	11	-2
-16	10	-9

5,3,L

15	18	-14
14	12	-11
13	21	-19
11	18	-17
10	33	36
9	72	-72
7	10	-10
6	44	-42
5	60	-64
4	23	26
3	37	36
2	15	12
1	20	-20
0	25	28
-1	63	-67
-2	27	30
-3	56	-55
-4	10	6
-5	29	-28
-6	22	-24
-7	63	-61
-8	23	-20
-9	12	-4
-10	80	-81
-11	54	-54
-12	32	-31
-13	31	34
-14	20	22
-16	13	-17
-18	35	30

5,2,L

13	12	-11
12	34	36
11	17	-23
10	21	-22
9	82	77
8	33	-33
7	30	-29
5	12	-13
4	99	98
2	15	20
1	49	-47
0	13	-14
-2	33	-35
-3	34	32
-4	22	-21
-5	25	-21
-6	49	48
-7	148	150
-8	43	-44
-9	48	46
-10	73	71
-11	21	18
-12	32	31
-13	34	34
-14	55	58
-16	11	6
-17	13	10
-18	22	-14
-19	17	12

5,1,L

18	13	0
14	14	-12
13	19	-18
12	77	-74
11	88	88
9	57	-55
8	60	59
7	28	-26
6	41	39
5	24	25
4	80	79
3	59	59
2	21	14
1	20	23
0	30	28
-3	33	31
-4	53	-54
-5	91	91
-6	22	-23
-7	112	110
-8	142	141
-9	83	-83
-10	15	15
-11	11	-12
-12	28	30
-13	26	27
-15	22	-24
-16	11	-9
-19	20	-22

5,0,L

18	23	-19
16	24	-20
14	35	-33
12	32	32
10	121	112
8	44	-43
6	14	-18
4	33	29
2	54	-49
0	43	-42
-2	69	-69
-4	94	-92
-6	214	209
-8	161	-157
-10	81	-79
-12	52	-53
-14	26	26
-16	25	22
-18	17	-13

4,8,L

9	24	29
8	16	-16
7	32	-35
6	31	-32
-1	15	16
-4	20	24
-7	51	53
-8	13	12
-9	32	-30

4,7,L

11	22	20
10	23	26
9	15	10
8	48	-52
7	49	-52
6	13	12
5	21	24
4	11	14
3	11	13
2	11	9
1	19	18
-1	22	23
-3	49	-51
-4	27	-28
-5	17	15
-6	25	-31
-8	19	-23
-9	55	-54
-10	42	-39
-11	12	14
-12	37	35
-13	11	7

4,6,L

14	25	-22
13	11	5
9	58	-59
8	61	-64
7	56	-54
6	27	32
5	35	-33
4	25	-26
3	11	-13
2	12	-4
1	18	-21
0	10	10
-1	17	-18
-2	46	-49
-3	15	-15
-4	32	-37
-5	10	-8
-6	25	26
-7	26	-28
-8	26	27
-9	64	-64
-10	28	28
-12	42	44
-13	15	-15
-14	14	11

4,5,L

16	18	-16
15	31	-33
14	16	-19
13	22	-21
11	22	-19
8	21	21
7	54	-58
6	55	56
5	50	52
4	14	-7
3	20	17
2	25	25

4,5,L

1	28	32
0	13	9
-1	20	24
-2	56	-56
-3	60	-63
-4	74	80
-5	23	22
-6	51	51
-8	27	24
-9	40	-39
-10	36	39
-11	12	9
-12	34	-36
-13	22	-23
-14	12	12
-18	12	-9

4,4,L

18	13	7
15	15	-16
13	44	44
12	51	50
11	36	37
10	52	54
7	159	162
6	84	-85
5	86	87
3	82	83
0	12	11
-1	37	-37
-2	58	-58
-3	26	28
-4	57	56
-5	98	102
-6	14	-12
-7	42	44
-8	76	79
-9	93	98
-10	80	-82
-11	104	103
-12	62	61
-13	45	43
-14	14	14
-15	14	10
-16	12	17
-17	23	25

4,3,L

19	12	13
15	12	-12
14	25	27
12	10	13
11	16	-13
10	81	-80
9	137	141
8	149	-151
7	36	-36
6	34	33
5	28	28
4	32	33
3	11	-9
2	30	-30
1	67	68
0	33	36
-1	36	40
-2	15	22
-3	47	46
-4	127	126
-6	19	-18
-7	10	12
-8	116	-120
-9	35	32
-10	48	50
-11	104	-107
-12	12	15
-13	10	-10
-14	24	-25
-15	27	-26
-16	27	-29
-18	33	-31

4,2,L

19	39	-39
17	14	-14
16	14	-14
13	26	29
12	23	-25
11	26	30
10	16	-14
9	62	-63
8	137	141
7	51	-49
6	11	10
5	34	35
4	33	-34
3	111	-116
2	40	-41
1	62	-64
-1	109	-108
-2	14	15
-3	53	-52
-4	20	-21
-5	143	-144
-6	89	-93
-7	100	-104
-8	141	145
-9	229	-243
-10	51	-54
-11	21	24
-12	78	-79
-13	22	-21
-14	121	-129
-15	17	-14
-16	23	23
-17	30	33
-19	17	-16
-20	17	14

4,1,L

21	24	-22
17	20	21
14	10	7
13	14	14
11	39	-39
10	62	63
9	16	15
8	39	-38
7	25	-29
5	68	-69
4	69	-71
3	171	-178
2	93	-94
1	100	100
0	49	47
-1	77	-74
-2	13	12
-3	58	-61
-4	35	35
-5	15	-12
-6	112	116
-7	31	-32
-9	182	190
-10	44	-39
-11	10	12
-12	18	-15
-13	10	-20
-14	47	-48
-15	34	37
-18	16	-13
-19	10	9
-21	18	-22

4,0,L

20	32	-35
18	32	30
16	18	-15
14	38	-38
12	19	-14
10	71	-66
8	20	-17
6	33	-37
4	53	-51
2	268	273
0	167	168
-2	48	47
-4	91	-91
-6	93	-93
-8	83	-81
-10	45	47
-12	16	15
-14	18	17
-16	106	120

3,9,L

3	12	-9
0	39	38
-1	18	23
-5	26	-28
-8	33	-37

3,8,L

12	18	-19
11	25	24
10	23	-23
9	11	-12
8	46	-44
6	17	16
4	15	-13
3	37	-38
2	10	-1
0	21	22
-2	17	-16
-3	22	-24
-5	26	27
-6	37	-39
-7	20	18
-8	25	-23
-10	42	45
-11	47	50

3,7,L

14	28	-28
13	11	10
12	15	-18
11	11	-11
10	19	-22
9	28	-31
8	16	14
7	98	105
6	91	94
5	46	-51
4	37	34
3	46	47
1	22	21
0	38	38
-1	26	26
-3	34	37
-4	11	-3
-6	29	30
-8	11	5
-9	46	47
-10	76	74
-11	47	47
-12	24	-22
-13	32	-35
-14	35	-35
-15	13	0
-16	18	-17

3,6,L

17	20	17
14	11	10
13	10	6

3,6,L

10	45	43
9	18	21
8	123	130
7	50	57
6	103	107
4	139	-138
3	56	58
2	12	-13
1	23	23
-2	26	-26
-4	9	2
-5	16	-17
-6	34	-36
-7	26	27
-8	28	-29
-9	71	71
-10	98	96
-11	10	12
-12	164	-164
-13	34	35
-14	22	21
-17	22	16
-18	25	25

3,5,L

15	10	-11
14	12	13
13	11	-10
12	13	15
11	35	-36
10	22	24
9	54	-55
8	50	54
7	95	100
6	250	-262
5	207	-219
4	23	-24
3	75	-78
2	14	-14
1	85	-88
0	22	22
-1	33	33
-2	9	-14
-3	81	82
-4	20	-20
-5	20	-23
-6	16	-18
-7	11	-18
-9	23	-25
-10	86	-88
-11	46	-47
-12	80	-78
-13	145	-145
-14	70	67
-15	48	-47
-16	14	12
-17	10	-13
-19	22	-20

3,4,L

19	20	-16
17	44	-46
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2,8,L

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2,3,L

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2,2,L

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9	92	88
8	96	89
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2	76	-70
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16	160	-163
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14	181	-183
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10	79	-81
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4	370	360
2	153	161

Table XXI 1-Isopropyl-2-naphthyl acetate: Final structure factors

The table shows:

H^* $|F_o|$ $|F_c|$ Phase(°)

* Reflections sorted into groups with common K,L indices (shown in each group heading)

Values of $|F_o|$ with the suffix L are "unobserved".

H,0,0

2	139	67
4	1417	-1491
6	974	-1010
8	794	-811
10	120	-129
12	0L	0
14	263	252
16	106	-105
18	52L	0
20	168	163
22	0L	-19

H,0,2

0	880	-901
1	356	365
2	531	531
3	493	-490
4	722	726
5	1191	-1204
6	795	-792
7	93	99
8	401	-400
9	171	170
10	388	371
11	521	519
12	222	236
13	58	-59
14	0L	21
15	106	-102
16	0L	-4
17	152	-142
18	14L	35
19	0L	13
20	194	-184
21	169	181
22	60L	-73

H,0,4

0	713	723
1	781	793
2	672	668
3	92	-97
4	800	-793
5	347	338
6	547	538
7	586	591
8	173	-176
9	26L	61
10	462	-463
11	20L	29
12	117	97
13	59	-75
14	19L	-10
15	71	-106
16	16L	16
17	91	-80
18	11L	-59
19	90	-98
20	109	112
21	97	-87
22	70	65

H,0,6

0	165	175
1	185	191
2	541	549
3	55	-62
4	0L	-27
5	286	282
6	772	-792
7	80	-79
8	163	139
9	129	127
10	271	279
11	252	-260
12	77	79
13	115	104
14	224	-244
15	128	134
16	99	-110
17	183	-186
18	36L	27
19	76	68
20	0L	28
21	5L	31

H,0,8

0	622	617
1	190	192
2	124	110
3	30L	64
4	0L	13
5	77	-66
6	420	-423
7	332	323
8	38L	-53
9	22L	-44
10	0L	30
11	0L	3
12	0L	-6
13	99	-106
14	162	179
15	98	-101
16	127	140
17	114	115
18	86	-74
19	49L	-39
20	84	-72

H,0,10

0	124	115
1	279	-278
2	285	286
3	148	172
4	381	-399
5	180	193
6	211	-216
7	120	-114
8	60	61
9	24L	58
10	126	125
11	184	179
12	114	128
13	66	82
14	48L	-20
15	119	-130
16	49L	-18
17	123	-118
18	26L	-27
19	87	-78

H,0,12

0	71	-73
1	14L	34
2	181	179
3	39L	-50
4	0L	8
5	191	-207
6	114	-129
7	47L	-31
8	89	-77
9	270	294
10	35L	-12
11	28L	43
12	40L	69
13	62L	-11
14	45L	-14
15	100	-89
16	33L	-52
17	42L	-28

H,0,14

0	50L	14
1	325	-318
2	349	-364
3	207	-210
4	0L	8
5	175	172
6	173	171
7	0L	-2
8	106	101
9	45L	22
10	132	133
11	0L	27
12	0L	-18

H,0,14

13	35L	14
14	50L	7

H,0,16

0	122	136
1	195	211
2	82	-37
3	177	187
4	44L	-63
5	28L	-10
6	0L	-14
7	0L	41
8	0L	29
9	0L	-32
10	59L	61
11	0L	-17

H,0,18

0	58L	26
1	69	-3
2	31L	19
3	72	-79
4	94	-67

H,1,0

2	1088	1097
4	370	367
6	718	721
8	412	-418
10	361	-373
12	346	-347
14	147	137
16	314	310
18	40L	55
20	222	-213
22	0L	12

H,1,1

1	427	417
2	1420	-1451
3	775	789
4	531	-522
5	1115	-1123
6	365	-394
7	152	-138
8	75	76
9	129	-132
10	27L	-30
11	235	247
12	93	97
13	145	141
14	66	66
15	31L	-54
16	49L	6
17	31L	19
18	178	194
19	94	-101
20	22L	-41
21	59L	39
22	72	-71

H,1,2

1	1172	1182
2	74	-82
3	1003	-947
4	1848	1947
5	602	-602
6	445	434
7	407	-412
8	304	-286
9	225	218
10	83	-83
11	186	200
12	72	-67
13	169	185
14	138	-126
15	26L	-22
16	109	-102
17	55L	39
18	0L	33
19	59L	-69
20	89	93
21	70	-68
22	0L	-29

H,1,3

1	128	125
2	230	-236
3	930	-909
4	585	582
5	260	-255
6	372	-377
7	44	42
8	271	258
9	356	346
10	19L	17
11	174	191
12	104	-89
13	39L	52
14	50L	36
15	57	32
16	112	-108
17	14L	-40
18	0L	-26
19	38L	28
20	0L	-22
21	52L	-65
22	99	72

H,1,4

1	102	-110
2	543	538
3	82	-91
4	226	-227
5	203	191
6	550	-538
7	119	-99
8	294	283
9	271	-277
10	120	123
11	51	-9
12	162	164
13	200	208
14	122	-128
15	72	75
16	34L	6
17	0L	-11
18	53L	-34
19	37L	14
20	46L	-45
21	119	-112
22	72	23

H,1,5

1	383	384
2	171	170
3	80	77
4	0L	-7
5	81	-77
6	109	-101
7	564	-558
8	112	-91
9	91	99
10	0L	9
11	63	35
12	166	172
13	34L	-56
14	0L	3
15	39L	41
16	15L	4
17	32L	-54
18	27L	-44
19	0L	-8
20	0L	-43
21	0L	13

H,1,6

1	255	-260
2	101	117
3	554	-541
4	276	263
5	308	290
6	232	225

H,1,6

7	279	267
8	106	-106
9	74	-70
10	43L	-12
11	224	225
12	0L	-26
13	34L	-58
14	69	65
15	0L	24
16	67	-73
17	84	-79
18	0L	-23
19	40L	-20
20	45L	26
21	57L	41

H,1,7

1	491	475
2	438	-426
3	280	-277
4	130	-106
5	308	-296
6	33L	13
7	0L	-24
8	63	-68
9	0L	21
10	6L	28
11	172	168
12	29L	-16
13	100	100
14	76	-78
15	101	-92
16	82	71
17	31L	-49
18	96	95
19	52L	37
20	0L	24

H,1,8

1	299	-287
2	370	367
3	168	162
4	180	-188
5	109	-99
6	165	169
7	45L	-24
8	47L	-87
9	104	116
10	95	-83
11	0L	16
12	123	-117
13	107	117
14	96	98
15	62	-95
16	69	62
17	0L	19
18	61L	-14
19	0L	16
20	64L	4

H,1,9

1	76	78
2	197	184
3	86	-84
4	96	-105
5	55	-51
6	196	-210
7	69	-66
8	53L	61
9	39L	45
10	54L	49
11	21L	45
12	41L	-9
13	0L	67
14	124	120
15	19L	49
15	37L	49
16	48L	-52
17	0L	8
18	38L	-76
19	0L	-6

H,1,10

1	120	99
2	179	170
3	180	-179
4	180	175
5	89	-92
6	99	90
7	41L	-32
8	51L	14
9	51L	34
10	217	-228
11	55L	1
12	55L	-24
13	63	50
14	0L	10
15	111	114
16	67	53
17	58L	32
18	0L	29
19	99	-96

H,1,11

1	209	211
2	73	-75
3	0L	-29
4	35L	-18
5	0L	-12
6	176	180
7	225	-235
8	87	-93
9	6L	37
10	34L	-6
11	62	75
12	60L	45
13	0L	-57
14	42L	-43
15	0L	-12
16	37L	-14
17	75	-42
18	16L	-12

H,1,12

1	63	57
2	22L	13
3	195	194
4	60	36
5	260	-272
6	244	-265
7	173	-180
8	89	-86
9	18L	34
10	56L	44
11	73	90
12	95	122
13	51L	50
14	82	61
15	85	65
16	50L	-13
17	36L	14

H,1,13

1	153	152
2	38L	18
3	76	-74
4	288	-292
5	168	-171
6	46L	-74
7	87	88
8	20L	8
9	30L	3
10	0L	56
11	0L	-3
12	19L	18
13	32L	17
14	50L	0
15	65	-39

H,1,14

1	42L	-42
2	65	-71
3	50L	-31
4	129	-143

H,1,14

5	0L	28
6	0L	-14
7	0L	7
8	51L	16
9	0L	-52
10	115	110
11	30L	-38
12	34L	22
13	62L	71
14	29L	-52

H,1,15

1	142	-154
2	73	54
3	156	146
4	47L	75
5	70	-40
6	52L	26
7	63L	37
8	0L	-4
9	0L	13
10	11L	-23
11	0L	43
12	41L	32

H,1,16

1	62L	-50
2	167	-178
3	75	48
4	0L	-18
5	0L	34
6	0L	-18
7	30L	-28
8	51L	-35
9	0L	27
10	68	29
11	48L	-30

H,1,17

1	133	140
2	0L	-46
3	0L	-10
4	68	56
5	68	-69
6	59L	-46
7	46L	-12
8	15L	16

H,1,18

1	48L	40
2	17L	57
3	53L	-72
4	19L	29

H,2,0

0	322	-339
2	180	-171
4	257	-233
6	348	342
8	274	254
10	81	96
12	212	-229
14	28L	61
16	232	-249
18	54L	-45
20	223	229
22	0L	-6

H,2,1

0	611	-615
1	583	592
2	0L	21
3	795	791
4	84	-81
5	198	-188
6	16L	-13
7	453	-447
8	41L	4
9	388	-381
10	0L	30
11	82	-84
12	227	237
13	138	147
14	210	203
15	107	120
16	121	-116
17	68	47
18	222	-222
19	51L	40
20	34L	-2
21	51L	0
22	40L	28

H,2,2

0	583	-593
1	748	763
2	540	-535
3	717	-737
4	394	396
5	297	289
6	315	-314
7	0L	-39
8	69	56
9	427	-425
10	541	548
11	96	-92
12	39L	-30
13	127	-130
14	82	-93
15	246	251
16	92	90
17	122	131
18	40L	-54
19	27L	-9
20	45L	-51
21	28L	29
22	62L	16

H,2,3

0	403	399
1	331	339
2	761	774
3	543	-531
4	62	58
5	207	209
6	505	-493
7	301	286
8	381	-376
9	112	-104
10	57	-60
11	143	-134
12	0L	0
13	86	-105
14	0L	-44
15	49L	56
16	140	143
17	41L	50
18	53L	28
19	0L	31
20	0L	13
21	49L	5
22	0L	-8

H,2,4

0	552	544
1	245	-229
2	70	67
3	242	245
4	661	-668
5	650	640
6	590	-595
7	217	-212
8	407	403
9	212	-209
10	73	-69
11	92	83
12	200	221
13	110	-103
14	59	64
15	27L	24
16	65	-70
17	36L	28
18	41L	42

H,2,4

19	0L	2
20	43L	-74
21	67	-48

H,2,5

0	416	-405
1	198	187
2	219	223
3	311	299
4	18L	36
5	88	-81
6	26L	-29
7	524	-532
8	324	307
9	141	-144
10	148	-138
11	140	144
12	84	-80
13	139	141
14	0L	-2
15	36L	86
16	41L	26
17	0L	-11
18	67	12
19	0L	-34
20	73	-48
21	0L	3

H,2,6

0	715	674
1	33L	-41
2	339	328
3	82	79
4	278	-264
5	537	-520
6	185	-187
7	133	-120
8	231	-242
9	45L	61
10	57	44
11	99	115
12	89	92
13	95	91
14	44L	-53
15	0L	-38
16	0L	3
17	52L	42
18	38L	-24
19	0L	-7
20	40L	31
21	37L	38

H,2,7

0	217	211
1	280	-270
2	228	231
3	395	397
4	42L	58
5	112	107
6	120	-104
7	73	-75
8	153	-146
9	129	-125
10	71	-60
11	113	-109
12	15L	18
13	85	87
14	0L	40
15	9L	-45
16	28L	-10
17	70	62
18	0L	-5
19	0L	10
20	0L	-1

H,2,8

0	463	-447
1	205	-177
2	84	-82
3	322	-319
4	29L	-37
5	0L	-47
6	211	215
7	222	-221
8	0L	16
9	87	85
10	99	94
11	55L	48
12	81	88
13	47L	6
14	75	-43
15	51L	35
16	0L	-2
17	0L	19
18	53L	-41
19	75	50
20	0L	15

H,2,9

0	198	200
1	64	-58
2	33L	12
3	187	191
4	31L	-32
5	40L	32
6	0L	-12
7	157	-154
8	69	-74
9	107	107
10	104	103
11	0L	-49
12	70	-56
13	77	-66
14	0L	-19
15	49L	1
16	31L	4
17	54L	49
18	0L	-11
19	0L	11

H,2,10

0	116	134
1	210	212
2	21L	-5
3	46L	32
4	95	-89
5	130	141
6	0L	25
7	123	136
8	149	143
9	153	-164
10	116	-101
11	118	-112
12	43L	49
13	53L	4
14	81	-61
15	13L	28
16	84	-85
17	59L	51
18	75	63

H,2,11

0	240	241
1	148	155
2	29L	52
3	103	93
4	96	96
5	172	179
6	42L	32
7	114	-107
8	215	-218
9	167	-182
10	196	-202
11	84	80
12	0L	2
13	55L	47
14	121	124
15	0L	-11
16	21L	27
17	0L	-23

H,2,12

0	261	267
1	46L	-46

H,2,12

2	118	116
3	210	212
4	15L	-31
5	84	-91
6	190	-184
7	88	-89
8	0L	-62
9	0L	-16
10	0L	36
11	172	-196
12	27L	-35
13	182	70
14	73	-52
15	97	94
16	55L	25

H,2,13

0	162	151
1	56L	28
2	41L	9
3	40L	-46
4	0L	-47
5	77	-83
6	87	-87
7	42L	58
8	48L	-43
9	61L	57
10	102	102
11	25L	-25
12	74	90
13	54	-24
14	70	-26
15	92	84

H,2,14

0	95	104
1	46L	-30
2	64	75
3	54L	38
4	49L	-51
5	0L	-1
6	119	-110
7	63	-42
8	33L	-47
9	23L	-45
10	64	52
11	8L	11
12	14L	-12
13	59L	43
14	117	105

H,2,15

0	91	87
1	0L	-6
2	15L	39
3	0L	29
4	31L	-43
5	22L	27
6	22L	27
7	51L	32
8	52L	8
9	23L	1
10	45L	-67
11	43L	65
12	65L	-52

H,2,16

0	141	129
1	109	101
2	0L	17
3	44L	-14
4	44L	23
5	28L	-6
6	0L	-23
7	38L	11
8	106	-91
9	43L	49
10	0L	20

H,2,17

0	113	-119
1	91	94
2	0L	-17
3	7L	20
4	91	68
5	33L	-65
6	53L	48
7	55L	-9

H,2,18

0	47L	-32
1	0L	-27

H,3,0

2	487	470
4	340	-321
6	1151	-1123
8	228	217
10	61	55
12	73	73
14	237	242
16	166	176
18	151	-141
20	16L	-44

H,3,1

1	253	250
2	457	448
3	31L	36
4	654	632
5	87	98
6	480	-465
7	276	281
8	38L	-44
9	0L	2
10	82	-99
11	98	-103
12	57	-69
13	188	-197
14	0L	-5
15	219	-225
16	49L	1
17	139	125
18	71	87
19	42L	60
20	66	32
21	39L	44

H,3,2

1	361	-349
2	34L	-14
3	174	167
4	241	244
5	179	-168
6	160	151
7	203	213
8	252	-247
9	140	133
10	110	-113
11	79	90
12	281	280
13	71	-75
14	96	-97
15	66	-76
16	223	-225
17	76	-84
18	80	84
19	37L	39
20	41L	26
21	0L	29

H,3,3

1	246	230
2	228	217
3	245	-234
4	189	197
5	74	-60
6	29L	-46
7	151	137
8	135	144
9	169	-167
10	288	-292

H,3,3

11	81	66
12	0L	39
13	128	134
14	98	88
15	0L	31
16	42L	-53
17	160	-161
18	38L	66
19	59L	43
20	32L	-10
21	0L	34

H,3,4

1	192	-192
2	293	291
3	54	44
4	178	153
5	725	715
6	246	-249
7	134	-162
8	58	64
9	145	-144
10	33L	-35
11	208	-219
12	279	-287
13	115	-110
14	248	253
15	100	91
16	114	108
17	66	28
18	12L	4
19	23L	39
20	0L	-27
21	43L	24

H,3,5

1	147	146
2	469	449
3	377	364
4	142	126
5	0L	-22
6	346	348
7	444	-452
8	264	289
9	48L	32
10	50L	-64
11	123	133
12	257	-257
13	196	-208
14	22L	-40
15	44L	-11
16	0L	-12
17	47L	40
18	32L	-48
19	41L	0
20	0L	12

H,3,6

1	430	417
2	314	300
3	110	-134
4	214	228
5	216	-202
6	241	241
7	220	-231
8	466	-482
9	331	340
10	211	-230
11	79	-84
12	162	169
13	21L	-2
14	29L	21
15	0L	31
16	82	86
17	45L	-12
18	51L	-24
19	0L	22
20	0L	-12

H,3,7

1	195	178
2	139	-134
3	17L	-20
4	100	-95
5	136	-141
6	0L	44
7	102	119
8	181	-190
9	104	106
10	19L	-13
11	249	-261
12	159	162
13	87	92
14	61	52
15	0L	-12
16	49L	-7
17	0L	-41
18	39L	7
19	38L	31

H,3,8

1	133	140
2	277	267
3	89	83
4	115	-105
5	74	-70
6	139	-144
7	95	-115
8	75	-84
9	159	-170
10	189	198
11	134	151
12	131	135
13	18L	1
14	126	-129
15	41L	23
16	0L	-5
17	0L	3
18	77	-66
19	0L	-44

H,3,9

1	215	-207
2	238	229
3	44L	24
4	238	249
5	0L	12
6	35L	73
7	65	-74
8	191	205
9	256	264
10	82	-82
11	162	160
12	147	-160
13	108	-123
14	67	-45
15	50L	-42
16	0L	3
17	19L	13
18	0L	-19

H,3,10

1	188	-192
2	101	-82
3	176	177
4	24L	-20
5	47L	16
6	56	57
7	275	291
8	22L	24
9	182	-190
10	67	61
11	164	-162
12	53L	-46
13	52L	48
14	67	-13
15	17L	-25
16	31L	-41
17	49L	12

H,3,11

1	111	107
2	32L	30
3	0L	18

H,3,11

4	270	275
5	57	-68
6	88	86
7	40L	9
8	162	-159
9	0L	-29
10	0L	30
11	81	-80
12	0L	5
13	0L	-38
14	36L	-72
15	53L	69
16	26L	13

H,3,12

1	31L	-38
2	108	111
3	0L	-24
4	97	101
5	44L	68
6	79	-49
7	0L	-25
8	93	-95
9	25L	69
10	74	-78
11	72	54
12	0L	55
13	85	-100
14	89	97
15	87	-78

H,3,13

1	49L	-13
2	110	111
3	0L	-20
4	21L	38
5	0L	-8
6	124	121
7	53L	-57
8	107	-105
9	25L	-54
10	50L	-54
11	117	111
12	0L	-52
13	23L	86
14	0L	2

H,3,14

1	0L	25
2	65	84
3	40L	-64
4	150	145
5	47L	-1
6	0L	10
7	73	72
8	60L	52
9	0L	0
10	24L	-43
11	51L	-55
12	0L	-51

H,3,15

1	88	85
2	34L	-36
3	57L	-40
4	55L	44
5	143	-132
6	40L	18
7	7L	-18
8	61L	39
9	0L	27
10	0L	15
11	50L	49

H,3,16

1	0L	-4
2	10L	51
3	26L	72
4	0L	-1
5	0L	0
6	37L	-6
7	43L	-50
8	60L	2
9	0L	-19

H,3,17

1	36L	22
2	30L	-15
3	0L	-36
4	30L	43
5	0L	-4

H,4,0

0	317	305
2	238	-231
4	357	337
6	152	131
8	240	-219
10	23L	16
12	38L	-32
14	20L	8
16	37L	32
18	0L	-29
20	28L	-36

H,4,1

0	15L	33
1	0L	20
2	488	-481
3	196	-197
4	95	89
5	225	227
6	196	169
7	159	-153
8	37L	-47
9	0L	8
10	192	208
11	240	240
12	13L	42
13	0L	29
14	76	-72
15	55L	-18
16	34L	-13
17	107	-111
18	0L	2
19	68	-62
20	0L	-13

H,4,2

0	386	370
1	50	46
2	270	260
3	0L	-9
4	345	-331
5	304	-306
6	291	-283
7	0L	-31
8	104	108
9	26L	18
10	23L	-55
11	49L	50
12	0L	1
13	71	-32
14	79	60
15	90	96
16	0L	-23
17	0L	-10
18	34L	50
19	70	-54
20	0L	42

H,4,3

0	168	-148
1	247	250
2	279	-281
3	331	327
4	299	-288
5	79	83
6	320	326
7	81	85
8	386	379
9	75	88

H,4,3

10	80	-65
11	111	93
12	68	-87
13	139	-147
14	80	-89
15	49L	-59
16	73	-67
17	80	-41
18	42L	57
19	61L	-78
20	31L	24

H,4,4

0	527	-512
1	33L	-23
2	205	-187
3	83	-82
4	154	137
5	170	163
6	168	169
7	44L	37
8	28L	11
9	0L	13
10	169	175
11	164	175
12	92	97
13	29L	5
14	132	-133
15	197	-200
16	0L	-32
17	43L	-36
18	39L	-41
19	51L	55
20	45L	-13

H,4,5

0	487	-477
1	221	219
2	148	146
3	400	392
4	0L	-34
5	79	74
6	206	196
7	172	-166
8	78	-87
9	246	-252
10	128	-127
11	76	80
12	173	172
13	166	176
14	109	-119
15	89	-99
16	64	66
17	81	36
18	51L	43
19	0L	12
20	52L	-30

H,4,6

0	77	85
1	49	54
2	28L	31
3	64	73
4	0L	62
5	71	88
6	163	171
7	17L	39
8	16L	-25
9	134	135
10	305	-320
11	326	-330
12	115	-109
13	91	-93
14	79	50
15	180	181
16	33L	4
17	49L	29
18	69	44
19	45L	-20

H,4,7

0	131	-145
1	0L	29
2	80	-81
3	167	169
4	154	-167
5	107	-116
6	80	76
7	87	-84
8	63	69
9	216	235
10	0L	-25
11	216	-228
12	194	222
13	91	89
14	77	84
15	64	98
16	79	-86
17	77	-87
18	76	-69
19	0L	-11

H,4,8

0	113	126
1	0L	27
2	30L	-42
3	90	86
4	94	-92
5	104	105
6	233	-232
7	50L	-46
8	43L	61
9	294	-314
10	337	357
11	74	58
12	62	42
13	109	116
14	86	-88
15	0L	-7
16	49L	18
17	64L	47
18	15L	-5

H,4,9

0	0L	-10
1	60	-45
2	194	-194
3	81	-65
4	130	127
5	64	-49
6	83	-87
7	118	118
8	45L	48
9	0L	-12
10	183	203
11	11L	18
12	159	-167
13	95	110
14	49L	-16
15	90	-103
16	55L	19
17	42L	-73

H,4,10

0	188	190
1	47L	40
2	78	78
3	119	113
4	101	-98
5	34L	-22
6	70	16
7	29L	39
8	127	-113
9	141	161
10	134	-147
11	0L	5
12	68	83
14	105	110
15	23L	-49
16	38L	-12

H,4,11

0	171	-173
1	84	84

H,4,11

2	209	-215
3	123	105
4	47L	38
5	145	-143
6	203	200
7	127	-132
8	100	117
9	32L	-29
10	64	37
11	77	71
12	134	-142
13	69	35
14	46L	5
15	0L	52

H,4,12

0	163	-155
1	0L	-37
2	0L	28
3	151	-166
4	57L	58
5	64	-34
6	0L	-9
7	10L	33
8	33L	23
9	44L	-35
10	0L	14
11	0L	-12
12	46L	-9
13	76	70
14	40L	-45

H,4,13

0	276	-284
1	86	102
2	0L	14
3	52L	60
4	42L	18
5	66	60
6	0L	-17
7	29L	-42
8	75	94
9	104	-101
10	80	69
11	0L	-9
12	0L	-3
13	0L	0

H,4,14

0	74	72
1	0L	13
2	47L	-55
3	74	85
4	0L	-30
5	52L	29
6	0L	-13
7	65	-59
8	29L	-2
9	0L	4
10	70	52
11	26L	-20

H,4,15

0	46L	-10
1	0L	6
2	41L	-26
3	42L	28
4	35L	40
5	62L	75
6	47L	29
7	68	-80
8	11L	-31
9	0L	-32

H,4,16

0	35L	15
1	0L	-12
2	0L	-1
3	54L	-34
4	0L	-16
5	52L	6
6	32L	4

H,5,0

2	374	372
4	76	-55
6	25L	-25
8	111	-125
10	180	-186
12	56L	35
14	55L	36
16	69	22
18	7L	10

H,5,1

1	27L	-44
2	9L	12
3	241	230
4	94	-101
5	177	-178
6	91	74
7	205	-201
8	290	-287
9	60	-63
10	0L	37
11	98	99
12	159	165
13	65	67
14	0L	11
15	107	125
16	51L	-74
17	0L	-19
18	16L	14
19	95	-56

H,5,2

1	78	-73
2	104	-104
3	33L	40
4	182	170
5	92	-87
6	182	-202
7	79	-80
8	35L	-13
9	117	111
10	0L	24
11	0L	9
12	72	79
13	42L	53
14	46L	78
15	20L	-13
16	52L	-45
17	0L	47
18	0L	-16
19	66	-66

H,5,3

1	0L	-7
2	481	-480
3	282	-285
4	254	-261
5	0L	22
6	49L	-54
7	40L	-66
8	31L	33
9	99	108
10	166	181
11	74	71
12	21L	-59
13	148	142
14	72	82
15	34L	27
16	57L	48
17	0L	-62
18	74	-52
19	16L	-52

H,5,4

1	145	154
2	152	154
3	84	-81
4	145	127

H,5,4

5	51	46
6	75	-108
7	40L	-9
8	0L	16
9	23L	36
10	35L	0
11	143	-135
12	23L	43
13	10L	-21
14	50L	-33
15	0L	17
16	80	-101
17	73	-75
18	33L	-11
19	52L	83

H,5,5

1	111	-116
2	83	-84
3	15L	0
4	26L	-30
5	51L	-30
6	34L	33
7	80	75
8	58	57
9	191	201
10	42L	28
11	59	-71
12	91	80
13	113	-120
14	180	-182
15	66	-63
16	66	14
17	82	83
18	35L	8

H,5,6

1	167	-171
2	0L	3
3	27L	11
4	186	-195
5	259	279
6	135	-147
7	115	-117
8	158	-167
9	88	82
10	125	134
11	30L	55
12	87	90
13	156	-158
14	75	68
15	67	66
16	64	57
17	0L	-29
18	66	-50

H,5,7

1	23L	42
2	102	103
3	60	-77
4	82	97
5	102	108
6	227	-246
7	106	106
8	273	-273
9	304	-317
10	0L	-27
11	42L	37
12	125	113
13	78	81
14	72	64
15	48L	59
16	29L	60
17	47L	-20

H,5,8

1	130	-140
2	123	129
3	55L	-32
4	95	90
5	55L	9
6	251	251
7	254	248
8	153	-173
9	0L	38
10	28L	-15
11	101	-87
12	0L	-19
13	69	44
14	58L	-96
15	77	-73
16	45L	35
17	0L	-20

H,5,9

1	100	82
2	110	-116
3	84	79
4	163	-165
5	174	-181
6	81	81
7	117	-129
8	101	122
9	63	-45
10	0L	-2
11	121	134
12	138	-139
13	164	176
14	25L	68
15	33L	-38
16	0L	15

H,5,10

1	0L	35
2	105	104
3	86	81
4	56L	58
5	33L	-37
6	104	-108
7	0L	17
8	50L	-57
9	81	-69
10	30L	-27
11	14L	-4
12	41L	23
13	27L	-82
14	80	75
15	43L	-73

H,5,11

1	129	153
2	139	-142
3	73	-65
4	183	-195
5	60L	50
6	88	-58
7	72	-60
8	51L	64
9	0L	-11
10	20L	46
11	74	-74
12	89	90
13	0L	-59
14	0L	5

H,5,12

1	56L	-46
2	48L	11
3	0L	-19
4	111	125
5	0L	-4
6	56L	-73
7	74	89
8	13L	-45
9	0L	0
10	28L	-17
11	16L	-1
12	0L	15
13	0L	18

H,5,13

1	56L	-75
2	39L	-12

H,5,13

3	60L	25
4	47L	-43
5	53L	49
6	93	-114
7	82	52
8	44L	21
9	0L	7
10	62L	-4
11	57L	-49

H,5,14

1	0L	6
2	0L	47
3	0L	-29
4	37L	-5
5	47L	67
6	0L	14
7	32L	-5
8	0L	10
9	0L	-31

H,5,15

1	0L	19
2	42L	29
3	11L	38
4	68	-55
5	28L	-41
6	0L	24
7	0L	-21

H,5,16

1	14L	-30

H,6,0

0	107	-97
2	112	116
4	117	124
6	118	117
8	137	-133
10	241	-255
12	20L	17
14	48L	65
16	0L	15
18	23L	39

H,6,1

0	127	-123
1	75	79
2	174	190
3	193	197
4	37L	22
5	11L	-5
6	123	-132
7	146	-160
8	147	-145
9	130	-120
10	56L	0
11	78	-82
12	56L	37
13	53L	49
14	48L	44
15	70	53
16	0L	16
17	82	55
18	34L	46

H,6,2

0	185	195
1	0L	27
2	62	43
3	51L	40
4	83	-68
5	40L	-44
6	24L	-29
7	0L	4
8	32L	-47
9	29L	-17
10	59	27
11	116	-118
12	71	65
13	69	75
14	0L	-29
15	41L	52
16	24L	-6
17	57L	7
18	0L	-18

H,6,3

0	72	56
1	409	411
2	61	68
3	92	72
4	45L	-26
5	33L	-55
6	6L	7
7	62	-28
8	128	-141
9	78	-88
10	0L	8
11	0L	51
12	63	51
13	17L	23
14	67	67
15	47L	70
16	46L	60
17	62L	-55
18	143	-150

H,6,4

0	28L	51
1	72	-65
2	102	121
3	19L	11
4	20L	17
5	62	-18
6	134	-146
7	60	55
8	83	-89
9	104	105
10	49L	-35
11	0L	28
12	54L	62
13	36L	16
14	23L	56
15	85	-95
16	14L	34
17	53L	-53

H,6,5

0	0L	-6
1	290	-299
2	282	284
3	256	-266
4	77	89
5	117	130
6	252	-242
7	45L	-40
8	44L	18
9	37L	-62
10	103	-109
11	78	51
12	0L	-28
13	33L	24
14	98	-95
15	27L	21
16	52L	12
17	57L	9

H,6,6

0	52L	54
1	26L	3
2	17L	2
3	83	-90
4	78	80
5	93	-110
6	88	74
7	114	119
8	37L	-54
9	51L	67
10	88	-83
11	0L	-7
12	60L	-76

H,6,6

13	52L	10
14	71	56
15	0L	-6
16	0L	-4

H,6,7

0	58	-54
1	51L	68
2	136	-142
3	265	273
4	111	-108
5	199	-206
6	182	191
7	98	-108
8	223	232
9	58L	58
10	32L	16
11	0L	-35
12	77	-75
13	38L	68
14	77	-38
15	0L	-30
16	31L	-13

H,6,8

0	52L	-33
1	0L	-25
2	59	53
3	0L	-28
4	33L	48
5	0L	-15
6	147	-167
7	21L	-52
8	0L	-39
9	80	46
10	120	117
11	71	42
12	35L	-20
13	23L	23
14	38L	27

H,6,9

0	7L	4
1	56L	-49
2	77	74
3	286	307
4	157	150
5	283	286
6	0L	12
7	148	-146
8	208	-222
9	104	-105
10	0L	-22
11	0L	-36
12	85	-79
13	39L	28
14	60L	14

H,6,10

0	0L	-16
1	25L	-43
2	71	-49
3	111	-117
4	0L	28
5	0L	24
6	74	68
7	100	89
8	29L	15
9	68	68
10	53L	-54
11	82	83
12	39L	-8
13	0L	-48

H,6,11

0	216	214
1	129	136
2	50L	18
3	82	-76
4	45L	-58
5	0L	-39
6	16L	-41
7	28L	35
8	70	-47
9	0L	-43
10	54L	-29
11	56L	-13
12	69	61

H,6,12

0	69	-75
1	37L	-24
2	40L	21
3	0L	-27
4	68	46
5	49L	0
6	0L	-5
7	35L	8
8	0L	-9
9	0L	20
10	0L	3

H,6,13

0	52L	64
1	0L	-5
2	53L	-15
3	36L	31
4	10L	9
5	76	59
6	44L	-16
7	0L	11
8	37L	-14

H,6,14

0	47L	-8
1	0L	-12
2	42L	-6
3	28L	-10
4	68	-55
5	60L	22
6	43L	14

H,7,0

2	125	129
4	82	93
6	0L	11
8	60	-81
10	48L	38
12	0L	0
14	36L	-59
16	0L	18

H,7,1

1	44L	8
2	145	-146
3	108	-94
4	151	162
5	157	166
6	50L	-15
7	0L	18
8	159	-173
9	46L	47
10	0L	-49
11	110	-108
12	116	122
13	83	-71
14	59L	10
15	0L	-3
16	32L	5

H,7,2

1	135	-154
2	58	62
3	52L	8
4	200	203
5	55L	69
6	73	81
7	37L	46
8	60	-68
9	55L	-31
10	95	-91

H,7,2

11	45L	-23
12	62	-19
13	53L	69
14	0L	7
15	0L	10
16	57L	56

H,7,3

1	49L	-25
2	423	419
3	126	123
4	0L	-2
5	66	-41
6	45L	20
7	0L	-43
8	77	78
9	116	-113
10	43L	-61
11	27L	34
12	104	-97
13	64	85
14	92	-94
15	59L	31
16	82	75

H,7,4

1	253	249
2	134	135
3	173	-175
4	273	295
5	81	-78
6	46L	-24
7	49L	-45
8	0L	-5
9	0L	0
10	75	-62
11	0L	47
12	23L	-15
13	47L	20
14	18L	41
15	49L	-50

H,7,5

1	76	81
2	193	-200
3	39L	59
4	61	-53
5	0L	5
6	126	110
7	50L	-65
8	44L	-39
9	132	-155
10	27L	84
11	0L	14
12	0L	11
14	47L	63
15	62L	67

H,7,6

1	58L	-66
2	138	131
3	31L	-2
4	129	-126
5	98	93
6	55L	-33
7	62	-74
8	20L	-27
9	50L	-22
10	67	-23
11	79	43
13	63L	20
14	9L	29

H,7,7

1	70	-86
2	0L	-17
3	83	101
4	105	-90
5	0L	-20
6	45L	48
7	0L	-20
8	74	87
9	35L	72
10	24L	23
11	0L	-29
13	0L	7
14	0L	-34

H,7,8

1	0L	-24
2	68	88
3	82	-70
4	80	72
5	0L	-37
6	165	189
7	55L	56
8	38L	-69
9	27L	12
10	60L	-55
11	36L	24
12	45L	-5
13	10L	58

H,7,9

1	33L	-5
2	71	-58
3	109	-113
4	27L	-3
5	0L	26
6	56L	-48
7	125	115
8	30L	46
9	33L	10
10	22L	18
11	15L	-29
12	108	87

H,7,10

1	74	88
2	175	167
3	76	80
4	0L	-9
5	143	-151
6	107	-112
7	72	-66
8	0L	2
9	0L	-1
10	0L	-32
11	30L	18

H,7,11

1	157	-167
2	0L	39
3	138	135
4	113	124
5	0L	35
6	29L	-2
7	70	23
8	0L	14
9	66	-3

H,7,12

1	65	-75
2	106	-116
3	41L	9
4	0L	12
5	0L	17
6	0L	-12
7	0L	-21

H,7,13

1	48L	62
2	66	-22
3	76	-82

H,8,0

0	171	-157
2	76	72
4	0L	-26
6	36L	6

H,8,0

8	73	93
10	75	-54
12	51L	-7
14	0L	-55

H,8,1

0	153	151
1	57L	-47
2	238	-238
3	79	-103
4	78	-93
5	19L	31
6	178	184
7	40L	21
8	107	124
9	0L	14
10	56L	35
11	0L	-40
12	40L	-62
13	46L	13
14	36L	-24

H,8,2

0	316	-329
1	53L	-61
2	93	-84
3	32L	17
4	72	67
5	0L	19
6	85	76
7	75	-58
8	87	70
9	13L	18
10	51L	28
11	42L	-36
12	30L	20

H,8,3

0	127	-130
1	158	165
2	16L	6
3	291	298
4	75	73
5	63	69
6	58L	-66
7	55L	-55
8	58L	46
9	75	-95
10	0L	34
11	38L	-9
12	28L	-59
13	0L	-2

H,8,4

0	24L	48
1	109	-97
2	64	-57
3	0L	14
4	9L	36
5	39L	55
6	7L	38
7	27L	-19
8	27L	-37
9	40L	-10
10	0L	-12
11	0L	-17
12	31L	-67
13	35L	-7

H,8,5

0	56L	54
1	34L	47
2	37L	82
3	34L	31
4	79	-84
5	12L	37
6	5L	25
7	36L	18
8	46L	-49
9	119	-110
10	26L	-28
11	56L	-14
12	63L	62

H,8,6

0	20L	-28
1	35L	-28
2	70	-81
3	31L	20
4	39L	-23
5	47L	-50
6	45L	60
7	73	-69
8	40L	55
9	45L	-24
10	0L	37
11	24L	35
12	49L	22

H,8,7

0	44L	-46
1	73	-20
2	19L	40
3	52L	44
4	29L	-17
5	17L	24
6	58L	-63
7	0L	-72
8	0L	-25
9	68	53
10	0L	-3
11	89	-81

H,8,8

0	32L	-59
1	34L	-1
2	69	-38
3	0L	-24
4	78	73
5	52L	-11
6	90	87
7	0L	4
8	0L	-61
9	34L	12
10	92	-78

H,8,9

0	95	81
1	43L	17
2	32L	-26
3	27L	-1
4	47L	38
5	41L	2
6	58L	-54
7	66	39
8	0L	-17

H,8,10

0	22L	8
1	0L	8
2	53L	-61
3	0L	-43
4	67	-11
5	0L	14
6	0L	53

H,8,11

0	114	106
1	66	-65
2	27L	-1
3	41L	-41

H,9,0

2	0L	0
4	209	-204
6	147	-157
8	0L	21
10	37L	45

H,9,1

2	132	-128
3	0L	-8
4	151	-175
5	65	91
6	152	156
7	0L	-32
8	61L	11
9	66	-38
10	0L	-34

H,9,2

1	119	-127
2	16L	14
3	65	73
4	72	41
5	60L	-13
6	43L	62
7	67	75
8	0L	-15
9	56L	6
10	28L	-53

H,9,3

1	67	-62
2	14L	15
3	0L	-43
4	46L	-48
5	70	64
6	0L	6
7	88	80
8	51L	17
9	70	43
10	66	72

H,9,4

1	82	75
2	38L	-14
3	69	33
4	41L	-10
5	0L	-14
6	70	-39
7	49L	-46
8	47L	-21
9	32L	-19

H,9,5

1	90	-96
2	79	74
3	33L	39
4	21L	22
5	37L	32
6	66	-18
7	137	113
8	74	-60

H,9,6

1	60L	20
2	29L	-22
3	0L	5
4	0L	4
5	0L	-2
6	45L	-2
7	0L	-51

H,9,7

1	57L	-30
2	0L	23
3	53L	3
4	73	45
5	57L	36
6	0L	24

H,9,8

1	43L	18
2	0L	-34
3	45L	10
4	36L	26

H,10,0

0	55L	76
2	0L	43
4	74	-55

H,10,1

0	46L	0
1	0L	-38
2	0L	-50
3	51L	47
4	97	-78

H,10,2

0	20L	-26
1	0L	-44
2	29L	15
3	26L	49

H,10,3

0	64L	35
1	37L	2
2	0L	21

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PART II

MOLECULAR MECHANICS

CHAPTER FOUR

Molecular mechanics: An introduction

4.1 Introduction

Much of the progress in organic chemistry in the last 100 years has in some way been connected with an increased understanding of the spatial requirements of molecules. It has also become clear that the chemistry of a compound is very much related to its structure and hence its "structural energy". A knowledge of these is quite clearly very desirable when forecasting the outcome of chemical reactions and particularly when allied to similar information regarding possible intermediates. These various differences in reaction rates, pathways and products have been explained qualitatively by the principle of 'tendency towards minimum energy' borrowed from the mechanical world. From this the concept of strain evolved and the requirement for a reliable quantitative basis. Experimental procedures did not appear to be able to supply the necessary data either because of limited applicability (diffraction and spectroscopic methods) or because of a distinct shortage of accurate work (thermochemical methods). On the theoretical side, quantum mechanical equations were too complex to solve in the short term and semi-empirical quantum mechanics, relying on geometries from other sources, evolved.

Molecular mechanics (MM) calculations currently provide the most accessible method. In essence the MM technique regards molecular systems as being composed of particles held together by harmonic forces. Suitable

potential functions are used to make these forces represent the different interactions occurring between the constituent atoms. The total molecular energy may then be minimised with respect to the geometry by balancing the various potentials involved.

Although the molecular mechanics method is not as sophisticated as the quantum mechanical approach, it can serve as an interim guide to correlating structure, energy, reactivity, and other molecular properties until such time as quantum mechanics is able to compete with regard to computer time. It must be stressed that MM is a model only and **Altona** (1) for instance, sees it as a natural extension to mechanical models, the short comings of which are well known. The major limitation of MM is its dependance upon empirical data.

4.2 Potential functions

The total steric energy Es in any isolated molecule may be defined in terms of various contributors:

$$E_s = E_b + E_{nb} + E_a + E_t + E_{opbe} + E_q \qquad (1)$$

where E_s = total steric energy

E_b = energy arising from bond stretching interactions.

E_{nb} = " " non-bonded "

E_a = " " angle bending "

E_t = " " torsional "

E_{opbe} = " " out of plane bending "

E_q = " " coulombic "

Each of these contributors can be represented in terms of a potential function.

(a) Bond stretching

This type of deformation has a very obvious connection with the classical Hooke's law and if it is assumed that harmonic restoring forces are in operation for small changes in bond length then,

$$E_b = \tfrac{1}{2}k_b\,(lo - l)^2 \qquad (2)$$

where k_b = the bond stretching force constant.

lo = the "equilibrum" bond length for the two atoms concerned.

l = the actual bond length.

Under normal circumstances very little bond stretching is encountered and this is a consequence of the very high values for k_b (typically 200 - 1200 K.cal/mole $\mathbf{A}^{-2}$).

Hooke's law tends to overestimate the energy required for large stretching deformations and a cubic term may be inserted to compensate. This is discussed more fully under the heading of angle bending (below).

(b) Non-bonded interactions

Numerous functions have been proposed over the years to describe non-bonded interactions because many approximations are required in order to interpret experimental results and consequently, such data are sparse. Several examples of the fit between proposed functions and observations are given in an early paper by Hendrickson (2). The data for inert gases are the easiest to interpret and

it has been the usual practice to interpolate these to cover other atoms. Thus, C..... C non-bonded interactions have been obtained, from observations of neon atoms, by curve fitting techniques.

Van der Waals produced his corrections to the gas law in 1873 by assuming that two distinct non-bonded effects were taking place. These effects were due to short range repulsive forces $\underline{E}(R)$ and a longer range attractive tendency $\underline{E}(A)$. Thus:

$$Enb = E(R) - E(A) \qquad (3)$$

In terms of the Lennard-Jones function this becomes:

$$Enb = A/r^n - B/r^6 \qquad (n = 8,12) \qquad (4)$$

where $\underline{r}$ is the internuclear separation and $\underline{A}$ and $\underline{B}$ are constants.

An alternative expression was derived by Buckingham:

$$Enb = A \exp(-Br) - c/r^6 \qquad (5)$$

The equations (6) and (7) due to Hill (3) are preferred for practical use because they contain only two variables:

$$Enb = \varepsilon(r^1/r)^n - 2.0\varepsilon(r^1/r)^6 \qquad (6)$$

$$Enb = 8.28 \times 10^5 \varepsilon \exp(-r/0.0736r^1) - 2.25\varepsilon(r^1/r)^6 \qquad (7)$$

where ε = a force representing the ease or otherwise of moving the two non-bonded atoms.

r = interatomic distance.

r^1 = sum of the Van der Waals radii

For (n = 12) in equation (6) the two expressions yield curves which only differ significantly in the extreme repulsive part.

(c) Angle bending (Baeyer strain)

The basic equation is derived from Hooke's Law

$$E_a = \tfrac{1}{2} k_a (\theta o - \theta)^2 \qquad (8)$$

The terms being analagous with those in equation (2). Typical values for $\underline{k}_a$ are 0.02 K.cal per mole per degree^2. Comparison with values quoted above for $\underline{k}_b$ gives an indication of the relative ease with which bond angles may be deformed.

As mentioned previously, large deformations present problems particularly for the angle bending function. Incorporation of a cubic term to equation (8) will correct the deformation in some cases. Its exact form is empirical and probably force field dependant. For instance Schleyer (4) uses the following expression:

$$E_a = \tfrac{1}{2} k_a(\Delta\theta^2 - k^1_a \Delta\theta^3) \qquad (9)$$

where $\Delta\theta = |\theta - \theta_o|$

k^1_a = an additional force constant for the cubic term.

While Allinger (5) has included equation (10) in one of his force fields:

$$E_a = \tfrac{1}{2} k_a (\delta\theta^2 + k^1_a \delta\theta^3) \qquad (10)$$

where $\delta\theta = \theta_o - \theta$

The changes made to Hooke's Law by these two

approaches is illustrated in Figure 4.1

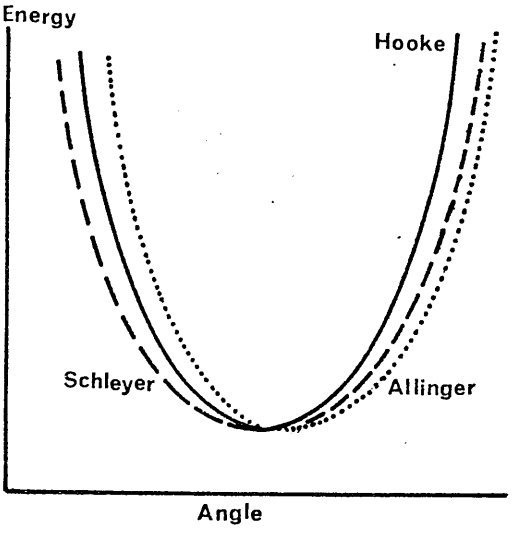

Fig. 4.1

Schleyer (4) has compared results from these two force fields and when large angle deformation is such that $\theta < \theta_o$ there is very little difference in the calculated angles. Boyd (6) has treated this situation as a separate system.

Further difficulties arise, however, when a force field is required to cope with $\theta \gg \theta_o$ as well. Fig. 4.1 shows quite clearly that if $\Delta\theta$ is used then the angle energy contribution will decrease (equation 9) on both sides of the equilibrium position. Conversely, $\delta\theta$ (equation 10) changes in opposite senses for positive and negative deformation. Ideally, a force field should be parameterised with a wide range of compounds representing both kinds of deformation (see section 4.3).

(d) Torsion (Pitzer Strain)

It is now well known that rotation about a single carbon-carbon bond is restricted and that eclipsed and staggered conformers correspond to different energy states. The exact physical nature of such barriers is still unclear and contemporary thinking tends to favour some combination of non-bonded repulsions and electron cloud interaction. The potential function used to represent torsional interactions is:

$$E_t = \tfrac{1}{2}k_t\ (1 + \text{sign.}\ \text{Cos}\, n\omega\ ) \qquad (11)$$

where k_t = torsional force constant.

The term (1+ sign. Cos $n\omega$) represents the particular torsional situation being studied. For instance in ethane, Fig. 4.2 the staggered conformation shown has the minimum torsional interaction (zero) and this situation occurs three times during a 360° rotation. The three-fold barrier is accounted for by setting n = 3 in equation (11) and 'sign = +1' allows for the staggered isomer being the minimum. Hence:

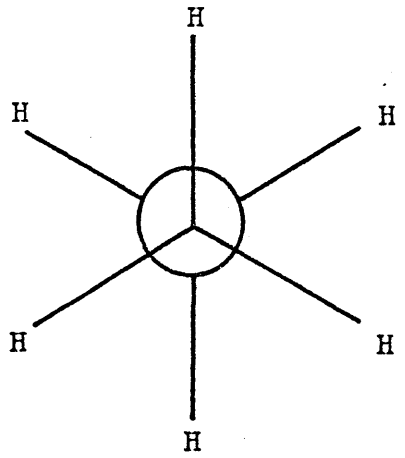

Fig. 4.2 Staggered ethane

$$E_t = \tfrac{1}{2}k_t\ (1+1.\ \mathrm{Cos}\ 3\omega) \qquad (13)$$

ω is the actual torsional angle which is 60° for any of the nine angles in Figure 4.2 and therefore:

$$E_t = \tfrac{1}{2}\ k_t\ (1+1.\ \mathrm{Cos}\ (3\times 60)) = 0$$

If an eclipsed conformation had been the minimum, as for example in propene then the three-fold barrier about the (C-C) bond would have 'sign = -1' and represent the situation shown in Figure 4.3.

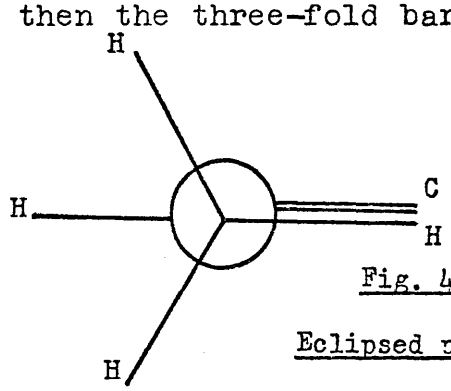

Fig. 4.3
Eclipsed propene

Equation (11) may be extended by the method of Wiberg and Boyd (7) to "drive" molecules to conformations other than the minimum so that, for example, pseudo-rotational pathways may be investigated. This is

achieved by means of equation (13).

$$E = k_t^1 . \tfrac{1}{2} . k_t (1 + \text{sign.Cos } n(\omega + \phi)) \qquad (13)$$

To return to the case of ethane, discussed above, the term $(1+\cos 3(\omega+\phi))=0$ for the minimum and hence:

$$\cos 3(\omega+\phi) = -1$$

giving $\underline{\omega+\phi = 60^\circ}$ as one of the solutions. Substitution of suitable values of ϕ therefore gives optimised energies for reaction co-ordinates other than those of the energy minimum,

If $\phi = 0^\circ$ $\omega = 60^\circ$ equivalent to equation (11)

$\phi = 20^\circ$ $\omega = 40^\circ$

$\phi = -20^\circ$ $\omega = 80^\circ$

The additional force constant $\underline{k}^1$ effectively makes the system pay a high penalty in terms of energy for any deviation from the $(\underline{\omega+\phi})$ minimum. Great caution is required in the selection of the value of $\underline{k}^1$. It will vary from conformation to conformation depending on, for instance, the proportion of the total steric energy contained in the torsional term concerned and on the change of energy with $\underline{\omega}$. The lowest possible value consistent with all the conformational considerations should be used. If $\underline{k}^1$ is too large then the calculated energies will be too high or at worst numerical instability will result. The most satisfactory means for determining $\underline{k}^1$ is by trial and error and if energy is plotted against reaction co-ordinate during the calculations then incorrect values of $\underline{k}^1$ soon become apparent*. Equation (13) is only used to obtain the conformation required and maintain it

* See section 5.2 for further discussion

during minimisation. The actual torsional contribution to the total steric energy is calculated from equation (11).

(e) Out of plane bending

At equilibrium the three bonds about a trigonal atom such as an sp^2 carbon lie in a plane. In some instances the total strain energy in a molecule may be reduced by these bonds assuming a non-planar geometry. If the improper torsion angle χ is defined as described by Warshel, Levitt and Lifson (8) then the following function may be used:

$$Eopbe = \tfrac{1}{2}\ kopbe\ (180 - \chi)^2 \qquad (15)$$

where kopbe is an appropriate force constant.

(f) Coulombic interactions

Some haloketones and cyclic peptides adopt certain conformations as a result of trying to get maximum separation between like polar groups. Most cases are not so extreme as this, but nevertheless it is preferable that such interactions should be considered in calculations on molecular systems in which they are present. A potential function of the form described in equation (16) can be used:

$$Eq = (Q1 \cdot Q2)/(332.17 \times D \times r_{1-2})\ K.cal.mole^{-1} \qquad (16)$$

where Q1, Q2 are the electrostatic changes in units of 'e' and r_{1-2} the interatomic separation. D should strictly be the value of the dielectric constant in the region of the dipoles but the magnitude of the local quantity is not determined easily and is probably best obtained by parameterisation (see 4.3).

(g) Interdependance of functions

Clearly in a real molecule the contributors to the total steric energy cannot be treated in isolation. One of the major differences between existing applications of the MM technique is in their attitude to cross-terms. It is easy to see that if, for instance, a bond angle is changed then the non-bonded contribution from the two extreme atoms will also change and similar effects exist between other functions. From the quantum-mechanical view point, of course, the cross-terms would be taken care of automatically.

In MM the Urey-Bradley (UBFF) based force field includes all non-bonded interactions while the valence force field (VFF) algorithm ignores 1,3- and in some cases 1,4- non-bonded terms. The UBFF approach requires no cross-terms while the VFF method, to a first approximation, relies on all the cross-terms being small and accounts for the excluded interactions in the other potential functions. More sophisticated VFFs (9) have added functions for stretch-stretch and stretch-bend interactions which become significantly larger in strained environments.

4.3 Parameterisation

Once the potential functions have been selected values must be obtained for force constants and equilibrium distances and angles. The order of magnitude of many force constants is available from spectroscopic work and some distances and angles can be gleaned from crystallographic

results. Apart from this there is not a great deal of basic information at hand. This has to some extent been overcome by a trial and error method in which unknown quantities are adjusted until experimentally observed criteria (e.g. geometries, energies) are reproduced. This approach is full of pitfalls and much care is required in order to produce a balanced force field.

It is crucially important to decide what the ultimate application is to be before parameterisation is attempted. A force field (FF) which is designed to cover as many compounds as possible will not be able to give forecasts as accurate in detail as an FF based on the fewer compounds in that particular situation.

Thus to evolve an FF which can be applied in as many situations as possible, the molecules used for parameterisation should represent a balanced mixture of the different types of strain occurring.

The information which an FF is going to be required to reproduce must also be considered at this stage. Ideally the calculations should be able to obtain the physical quantities which quantum-mechanics might supply, for example:

(a) Energies: thermochemical, strain, conformational, barriers.

(b) Geometries: in crystals, along pathways, of different conformations.

(c) Vibrational: frequencies, amplitudes.

(d) Other: nmr shifts, chemical reactivity.

But again, compromise is necessary for practical purposes. Energies and geometries are probably the most important quantities from a conformational viewpoint, although attempts have been made (8) to produce consistent FFs incorporating vibrational frequencies as well.

Force field I (Appendix A) was parameterised by Miss M.J. Bovill of the Glasgow molecular mechanics group using 45 different compounds representing a balanced group of compounds for which reliable data were available. Gas phase heats of formation at 25°C were obtained by adding on group increments to convert the calculated steric energies. These increments were themselves made variables in a least squares procedure to minimise the differences between the calculated and observed heats of formation. For the 45 compounds the mean deviation in ΔH_f was 0.45 Kcal per mole.

The other FFs used in the work which follows were not so extensively parameterised but were felt to be capable of producing meaningful results. As the main interest was in the comparison of related molecules it might have been expected that the deficiencies would cancel out.

4.4 Minimisation

A parameterised FF is only capable of calculating the steric energy of a particular supplied geometry. In order to find the minimum steric energy of the isolated molecule some way must be found to allow the atomic co-ordinates to mutually adjust themselves so as to

balance the various interactions present. This may be accomplished by one of the available minimum seeking techniques.

These techniques are sometimes (10,11) referred to as 'hill climbing methods' because of their analogy to a man trying to descend a mountain on a foggy day to a specific position in a valley below. The remainder of this section is devoted to a discussion of minimisation methods.

Steepest descents

Intuitively this technique is very appealing because the minimum is sought by following the path which reduces the value of the variable being minimised. This is quite acceptable for static problems but in the dynamic multidimensional environment of MM difficulties may arise.

Steepest descents has been used by Wiberg (12) and Allinger (13-16). The energy was optimised with respect to the co-ordinates by adjusting each of the latter by some small amount in both senses and computing the resultant energy change. If an energy decrease was obtained then its value was stored and the co-ordinate returned to its unperturbed value and the process repeated until all the co-ordinates had been tested. Each atomic position was then adjusted in the direction of lower energy by an amount proportional to the partial derivative of energy with respect to the co-ordinate being moved. The cycle of testing and storing was then restarted and the whole procedure repeated until successive iterations lowered the energy by less than some prespecified amount.

The advantages of this method are that the atoms

most affecting the energy are moved the greatest amount and that 'saddle point' false minima are generally avoided. Other false minima occur, apparently fairly frequently (13,17), so that there is no absolute guarantee of reliability. Further convergence is slow, particularly if the relative weights given to the variables are not reasonably accurate and Allinger (13) has reported that the magnitude of the perturbing increment is very important with respect to the final values of torsion angles.

Pattern Search

This is very similar to steepest descents of which it may be considered a modification. The principle used is that once a valley has been found on the response surface then there is a reasonable chance that it will lead to the minimum. Steepest descents is able to locate such valleys but its ability to follow them is a function of the angle at which they are met. Pattern search was developed to surmount this problem (18).

Again co-ordinates are changed by some increment to find the direction of energy decrease but this time the disturbed co-ordinate is not restored to its original value once a lower energy position is found. The calculations then proceed to the next co-ordinate and are continued until the energy changes are sufficiently small.

Schleyer et al (19) have obtained lower energies than with steepest descents alone. Pattern search has the added advantage of being scale invariant but it can have problems locating the valleys initially and also with

following unusually shaped valleys (20). False minima are also very troublesome.

Parallel tangents

Parallel tangents is based on both the previous methods and attempts to overcome their disadvantages. From a starting point, two new locations of lower energy are sought and then the minimum on the curve through these three points is used as a new starting position. The calculation is continued until the energy changes are considered small enough.

The method has been used by Scott and Scheraga (21) and its major disadvantages are false minima and coping with curved valleys.

Non-simultaneous local energy minimisation

Allinger (22) assumed that in the area close to the minimum the potential energy surface may be represented by:

$$E = Ax^2 + By^2 + Cz^2 + Dx + Ey + Fz + G \quad (17)$$

where x,y,z are atomic cartesian co-ordinates and A to G are constants to be determined.

From a location close to the minimum another point of lower energy is found by steepest descents. The potential energy and the partial derivatives with respect to each cartesian co-ordinate are calculated and used to evaluate the constants in equation (17). If the derivative of the equation is set to zero then a new minimum position will be obtained for the atom. Successive iterations are carried out over all the atoms until the parameter shifts

are small. Allinger (22) quotes its major advantage as the saving in computer time.

Newton-Raphson Minimisation

The main difference between this and the preceding methods is that a direct solution is sought to a set of simultaneous linear equations. Iterative minimisation gives reproducible minima (1,19) and the occurrence of false minima is much less likely than with search procedures. Computer programs for calculating such direct solutions have been evolved and used by several workers (8,23,24,25). These programs have the additional advantages that quantities such as vibrational modes and thermodynamic functions may be calculated readily and that computing times are reasonable.

The MM calculations in this thesis were carried out using this technique and the following discussion is based on the program PECALC (25).

It is well known that for any continuous function $f(x)$ which has a differential coefficient at each point between $x = a$ and $x = a + h$:

$$f(a + h) = f(a) + hf^1(a) \qquad (18)$$

where $\underline{h}$ is small and $f^1(a)$ is the first derivative of the function.

This is a statement of the mean value theorem and it may be extended to give the Newton-Raphson method for obtaining the roots of a polynomial by assuming that some

estimate (a) of a particular root is sufficiently close to the correct value (a + h) that equation (18) holds. Then, since for a root: $f(a + h) = 0$:

$$0 = f(a) + hf^{1}(a) \qquad (19)$$

In practice many iterations are needed for a complex function and if a = x (trial) and a + h = x(new) then equation (19) becomes:

$$x(new) = x\ trial - f(a)/f^{1}(a) \qquad (20)$$

In MM it is the energy $\underline{E}$ which must be minimised with respect to co-ordinate and hence it is the stationary value of $\underline{dE/dx}$ which is sought so that the second order form of equation (20) is required:

$$x(new) = x(trial) - f^{1}(a)/f^{11}(a) \qquad (21)$$

where $f^{11}(a)$ is the second derivative of the function.

The situation in a real molecule is much more complex than this one - co-ordinate example since each of the constituent atoms has three co-ordinates and therefore the minimum of a multidimensional function is being sought.

Many iterations of the three dimensional analogue of equation (21) are required to obtain the minimum and if successive values of the cartesian co-ordinates are represented by x_k, x_{k+1}, then:

$$\underline{x}_{k+1} = \underline{x}_k - \underline{\underline{F}}^{-1}\ \nabla E(x) \qquad (22)$$

and the minimum corresponds to a solution of $\nabla E(x) = 0$. The form of the matrix $\underline{\underline{F}}$ in effect describes the minimisation technique in use e.g.:

$\underline{\underline{F}} = c\underline{\underline{I}}$ where $\underline{\underline{I}}$ is the identity matrix and c a properly selected constant gives the steepest descents method.

$\underline{\underline{F}} = \frac{\partial^2 E}{\partial x_i \partial x_j}$ $i, j \leqslant 3$ for each atom represents the three dimensional version of equation (21). (23)

This latter algorithm avoids the scaling problems inherent in the steepest descent approach. The calculations in Part II of this thesis have been based on equations (23). The required derivatives being calculated numerically from equation (1).

This method however, neglects co-operative movements of the atoms and may lead to errors. The energies and geometries obtained by this block diagonal calculation can be further refined by setting $\underline{\underline{F}} = \frac{\partial^2 E}{\partial x_i \partial x_j}$ $i, j = 1,3n$ where n = number of atoms . (24)

Equation (24) thus includes all the off-diagonal terms and converges rapidly on the minimum. The full matrix technique does not converge for a crude trial structure when the components of $\nabla E(x)$ are necessarily large and the procedure adopted has been to use equation (23) initially to obtain a solution close to the stationary value and then employ the full matrix equation to calculate the minimum.

This method in addition to giving greater safeguards against false minima also avoids the difficulty encountered by some workers with torsion angle adjustment (4, 12, 26, 27). A further advantage is the facility to

calculate vibrational data from the final matrix of second derivatives.

These vibrational frequencies $\underline{\nu}_i$ can be computed from their relationship to the atomic masses and potential energy. Thus, for an $\underline{N}$ atom molecule the (3N-6) vibrational frequencies are given by the eigen values of the matrix $M^{-\frac{1}{2}}\underline{\underline{F}}.M^{-\frac{1}{2}}$ where $\underline{M}$ is the diagonal matrix of atomic masses.

Equations (25) and (26) may then be used to calculate the vibrational free energy, Fvib, and the vibrational zero point energy $\underline{Evib}^{o}$ respectively.

$$Fvib = kT \sum_{i=1}^{3N-6} \ln\left[1-\exp(^{-h\nu_i}/kT)\right] \qquad (25)$$

$$Evib^{o} = \tfrac{1}{2}h \sum_{i=1}^{3N-6} \nu_i \qquad (26)$$

4.5 References

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CHAPTER FIVE

Conformational analysis of a series of cyclo-octadienes

5.1 Forward

Carbocyclic systems are generally classified into groups of compounds based on the number of atoms forming the ring. The 1885 strain theory of Baeyer attempted to account for the variation in properties of cycloalkanes on the basis of the internal angles required for a series of regular polygons. This approach assumed that the cycloparaffins were planar and predicted increasing strain from (and including) 6-membered rings upwards.

The thermodynamic data that we now have available (Fig. 5.1) shows that small rings (3- to 5-membered) and medium rings (7- to 11- membered) are the most strained. Baeyer's theory only accounts for the progression observed in the small rings and it is not until allowance is made for the possibility of puckering that the heats of combustion of the larger rings can be explained.

One of the puckered forms of cyclohexane has a heat of combustion of 157.4 K.cal per mole per - CH_2- group identical with the value for a straight chain alkane and this figure is also approached for the cyclic compounds with twelve or more atoms in a single ring. These large rings also closely resemble open chain paraffins. The anomalous heats of combustion of the medium ring carbocycles arise because such compounds cannot completely relieve the torsional strain by changing bond angles. In addition, there is usually some strain arising from trans-

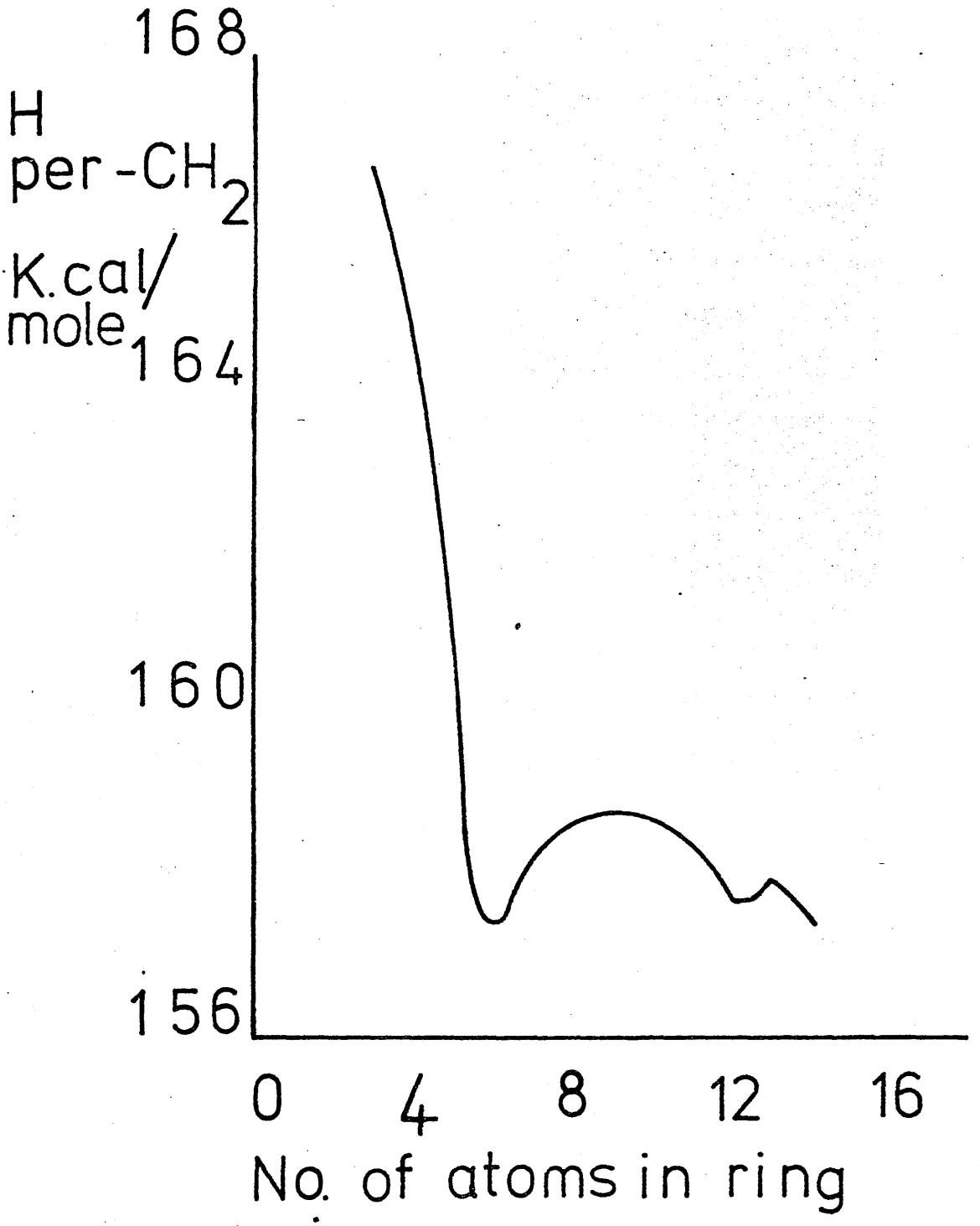


Fig. 5.1 Heats of combustion (H) of some cycloalkanes

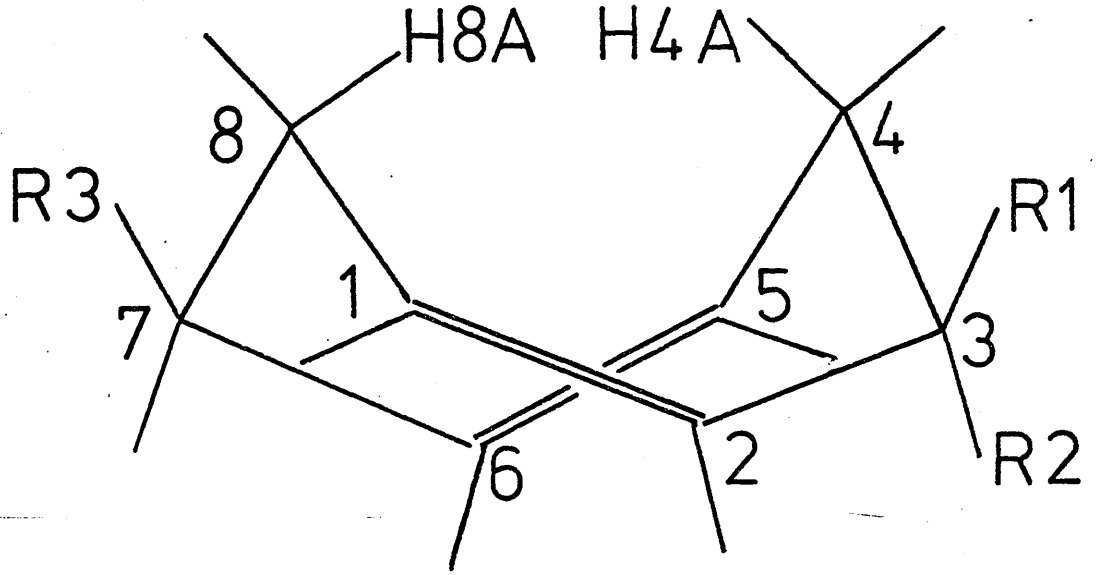
annular interactions.

Molecular mechanics (MM) by simulating the balance between these competing forces should be able to provide quantitative explanations of why one conformation is preferred over another in specific circumstances. The series of compounds studied in this chapter was selected because a previous investigation into a dibromo-octadiene had posed a number of interesting questions concerning the conformational processes which might occur in such a system. Also, the reported crystal structure of this particular compound provided sufficient data with which to check the reliability of the system to be used for subsequent calculations.

5.2 Introduction

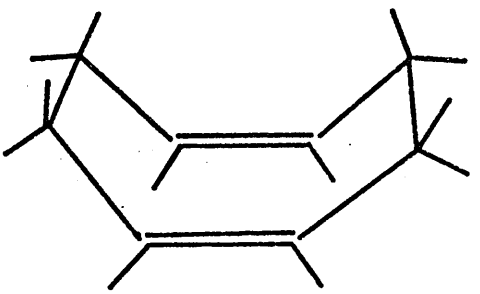
The conformations of cis, cis-cyclo-octa-1,5-dienes have been investigated by a number of workers. Dunitz and Waser (1) used geometric argu ments to show that both a rigid chair-like form and a family of flexible boats (Fig. 5.2) are possible for these dienes. In 1950 Roberts (2) made approximate calculations of the steric energies of the transition states between the boat, skew, and chair conformers of 1,6-dichloro-cyclo-octadiene. He suggested, on the basis of dipole moment measurements, that the boat was the most stable form.

The parent diene cis, cis-cyclo-octa-1,5-diene (COD) has been studied in the gas phase by electron diffraction

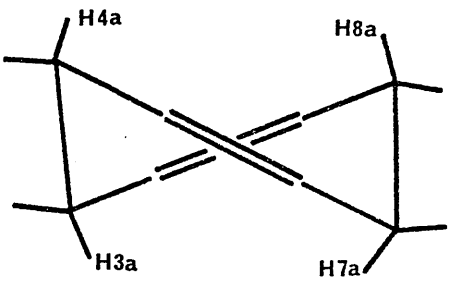


COD	R1=R2=R3=H
SDBCOD	R1=R3=Br, R2=H
ADBCOD	R1=H, R2=R3=Br
ADMCOD	R1=H, R2=R3=Me

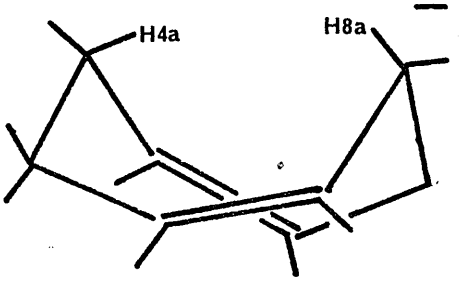
Boat C_{2V}

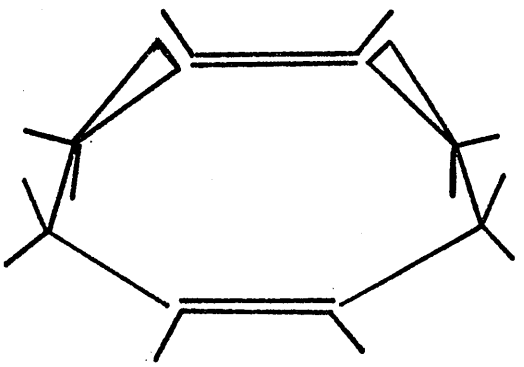


Skew D_2

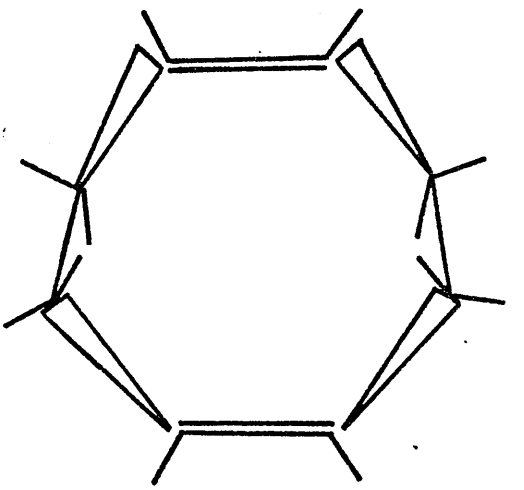


Twist-boat C_2





Transition state C_s



Chair C_{2h}

Fig. 5.2 COD: Major Conformations.

and this indicated that an equilibrium mixture of twist boat (most predominant) and chair conformers was present (3). Anet and Kozerski (4) determined the heights of the barriers to interconversion of the stereoisomers of COD by the variable temperature nmr technique and showed that the twist boat was the minimum energy form. Pauncz and Ginsburg (5) calculated that from consideration of only the H....H non-bonded interactions the boat of COD should be preferred to the chair. MM calculations (6,7,8) have suggested that the chair is more stable than the boat and that the twist boat represents the energy minimum. A number of x-ray analyses on metal complexes of COD have also shown a preference for the C_2 boat although this does not necessarily imply that the uncomplexed cyclo-octadiene should exist in the same conformation.

X-ray studies of (all ax-) -2,6-dimethylcyclo-octa-3,7-cis, cis-diene-1,5-dicarboxamide (15) and syn-3,7-dibromo-cis, cis-cyclo-octa-1,5-diene (SDBCOD)(16) found that both these derivatives of COD exist as twist boats in the crystalline state. Other physical techniques (nmr and ir spectroscopy and dipole moment measurement) have also been applied to SDBCOD in the solid and/or liquid phases (16). The results of these investigations have all indicated that the twist boat is the major conformer present in the solid and liquid states.

Dibenzocyclo-octa-1,5-diene (DBZCOD) has also been studied by x-ray diffraction and the eight-membered ring was found to have adopted the chair conformation (17). Recently, strain energy calculations (9, 18) have been

used to interpret the nmr spectrum of DBZCOD (19,20,21). The calculations explained the nmr spectra of both COD and DBZCOD in terms of an interconversion process between isoenergetic twist boats. The routes by which this can occur are discussed more fully in section 5.5. The differences between the preferred interconversion pathways of these two compounds were attributed to the distinct torsional barriers about the Csp^2 - Csp^3 bonds of the octadiene ring.

The preparation of anti-3,7-dimethyl-cis,cis-cyclo-octa-1,5-diene (ADMCOD) has been reported (22) and the conformational interconversion processes are currently being investigated by variable temperature nmr spectroscopy (23) using a sample kindly supplied by Professor Heimbach (Gesamthochschule Essen and Max-Planck-Institut fur Kohlenforschung).

The strain energy calculations in the literature (e.g. 7, 8, 18) have thus considered only the parent diene and derivatives such as DBZCOD which do not represent all the possible conformational situations arising during twist boat interconversion. In the work which follows the MM technique has been extended to include these other conformations for 3,7-disubstituted-derivatives of COD and the results compared with the available experimental data.

The latest Glasgow alkane/alkene FF(FFI) (24) was used for COD and ADMCOD while the less extensively parameterised FFII (24) was employed for SDBCOD and ADBCOD since FFI did not include any terms for interactions

involving the bromine atoms. Pseudorotation was achieved by the method of Wiberg and Boyd (25) and plots of energy against reaction co-ordinate (the C(2) - C(3) - C(4) - C(5) torsion angle) were used to check for false minima as described in Chapter 4. This approach does not necessarily give the true minimum energy for transition states because, even though there may be some regular change in energy as different constraints are imposed on the model, full relaxation is not possible. Ermer (26) has recently pointed out that when the torsion angle used as reaction co-ordinate is symmetrically located in relation to a two-fold axis of symmetry (2AS) in the nearest minimum structure, and this same symmetry element is not present in the transition state, then the method of Wiberg and Boyd will impose this 2AS on that transition state. One of the examples he cites in connection with this is the boat-chair transition state of cyclohexane. Wiberg and Boyd (25) used their "driving method" to calculate energies for the two transition states corresponding to $\underline{C}_2$ and $\underline{C}_s$ symmetry by assuming that four- and five- atoms were respectively coplanar and, (with a single C—C—C—C torsion angle as reaction co-ordinate)+ found that the former was preferred by about 0.5 K.cal $mole^{-1}$. Pickett and Strauss (27) on the other hand derived a pseudorotating transition state which incorporated both $\underline{C}_2$ and $\underline{C}_s$ forms implying that the energy difference between them was much smaller than that reported by Wiberg and Boyd. Ermer repeated the work of Wiberg and Boyd and obtained energies for the two transition states using the technique of removing the constraints at an appropriate mapping point. He obtained geometries which were close to, but not exactly corresponding to, the rigid four- and five- atom

+ for the $\underline{C}_2$ TS

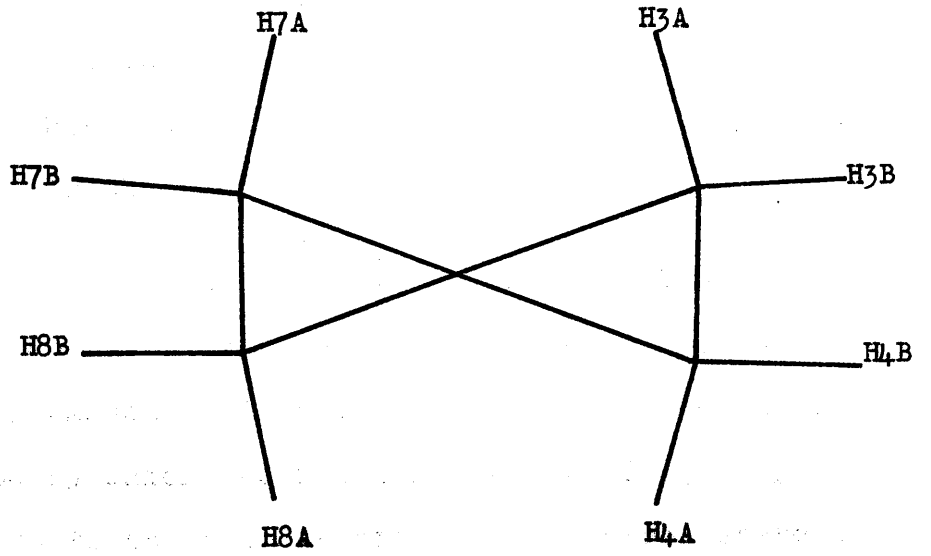
coplanar structures. Moreover the energy difference was now 0.00086 K.cal in favour of the C_s structure.

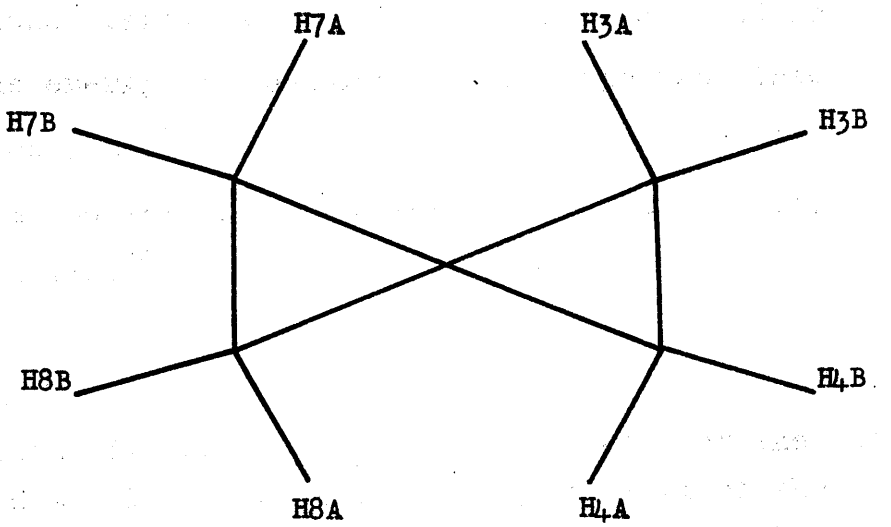
This result clearly indicates that caution is required when using mapping techniques to calculate conformational barriers. The calculations on cyclo-octadienes reported in this thesis constrained torsion angles which were symmetrically located about the C_2 axis of the global minimum and the possibilty therefore arises that the calculated transition states do not represent the true maximisations of the potential energy function, especially as the derivatives were calculated numerically. Therefore as a final check the constraints were removed from the models for the boat, skew, and boat-to-chair transition states of COD and ADMCOD. There was a reduction in energy in every instance, but in particular, the skew forms displayed drastic changes in both energy and geometry. The constrained (C) and non-constrained (NC) skew conformations of COD for example have an energy difference of over 6 K.cal per mole and this is sufficient to change the skew from being the least- to being the most-preferred intermediate between twist-boats*.

Ermer also discusses the relationship between the C_{2V} boat (B) and C_2 twist-boat of COD with respect to the calculations published by Allinger and Sprague (8, 28) and comments that

*The original calculations had constrained all nine torsion angles about the C(3)-C(4) and C(7)-C(8) bonds, thus 'locking' the conformation of the substituent hydrogens. It was found for COD that constraining the carbon skeleton only (e.g. C(2)-C(3)-C(4)-C(5)) gave essentially the same result as was obtained on subsequent removal of all the constraints. It appears that the fully constrained model (i.e. all nine torsion angles) is equivalent to Allinger's method of fixing the coordinates and has the same dire consequences.

(NC)





(C)

they initially described the former as a minimum (with respect to the $\underline{C}_{2h}$ chair; they did not consider the $\underline{C}_2$ twist boat) but correctly reported the $\underline{b}$ conformation as a transition state between twist boats in the later paper (8). However, in the same report they state that the boat is more stable than the skew, a result now shown to be incorrect for the reasons outlined above.

In some of the calculations which follow the variation in steric energy with reaction co-ordinate for the fully constrained model is illustrated and it is now clear that the method by which the results were obtained only allows conclusions to be drawn regarding the general shape of the energy versus torsion angle curves. Accordingly, the calculations for the dibromo-octadienes are only completely reliable as far as the geometries and energies of the non-constrained twist boats are concerned. In cases where the conformational barriers are of prime interest (COD and ADMCOD) the energy and geometry of the important intermediates have been obtained by using the mapping technique to approach the maximum and then removing the constraints to obtain full relaxation.**

**On occasions it was found that the geometry of the fully constrained model was not close enough to that of the transition state for convergence. In such cases the constraints were removed from the eight exocyclic torsion angles about the C(3) - C(4) and C(7) - C(8) bonds and a new stationary point sought with the block diagonal alogorithm. This new 'trial' geometry was then sufficiently close to the maximum for convergence to occur for the completely unconstrained system under full matrix conditions.

5.3 syn- 3,7- Dibromo - cis, cis-cyclo-octa-1,5 - diene (SDBCOD)

Method of calculation

The program PECALC (29) was used to minimize the steric energy in FFII (24) with respect to the atomic co-ordinates (16). The mathematical model was pseudo-rotated by the method of Wiberg and Boyd (25) and the minimum energy calculated at 10^{o} intervals throughout the pseudorotational pathway. Initially the block diagonal algorithm was employed for minimisation. Subsequently, the energies and geometries of important stereoisomers on possible interconversion routes were verified and refined by the full matrix calculation described in Section 4.4. The constraints were not removed during the final stages of refinement.

Results and Discussion

The study of SDBCOD by Mackenzie et al (16) reported the global minimum of this compound as being TB1 (Fig. 5.3). This has been confirmed by MM calculations and the geometry of this conformation is compared with the x-ray analysis in Table I* and serves as an indicator of the reliability of FFII.

*The geometric parameters cannot be compared rigorously because of errors inherent in the x-ray results (R = 11.1%). The possibility of differences between the calculated isolated molecule and the observed crystal structure must also be considered in this context.

Fig. 5.3 SDBCOD: Variation of energy with conformation

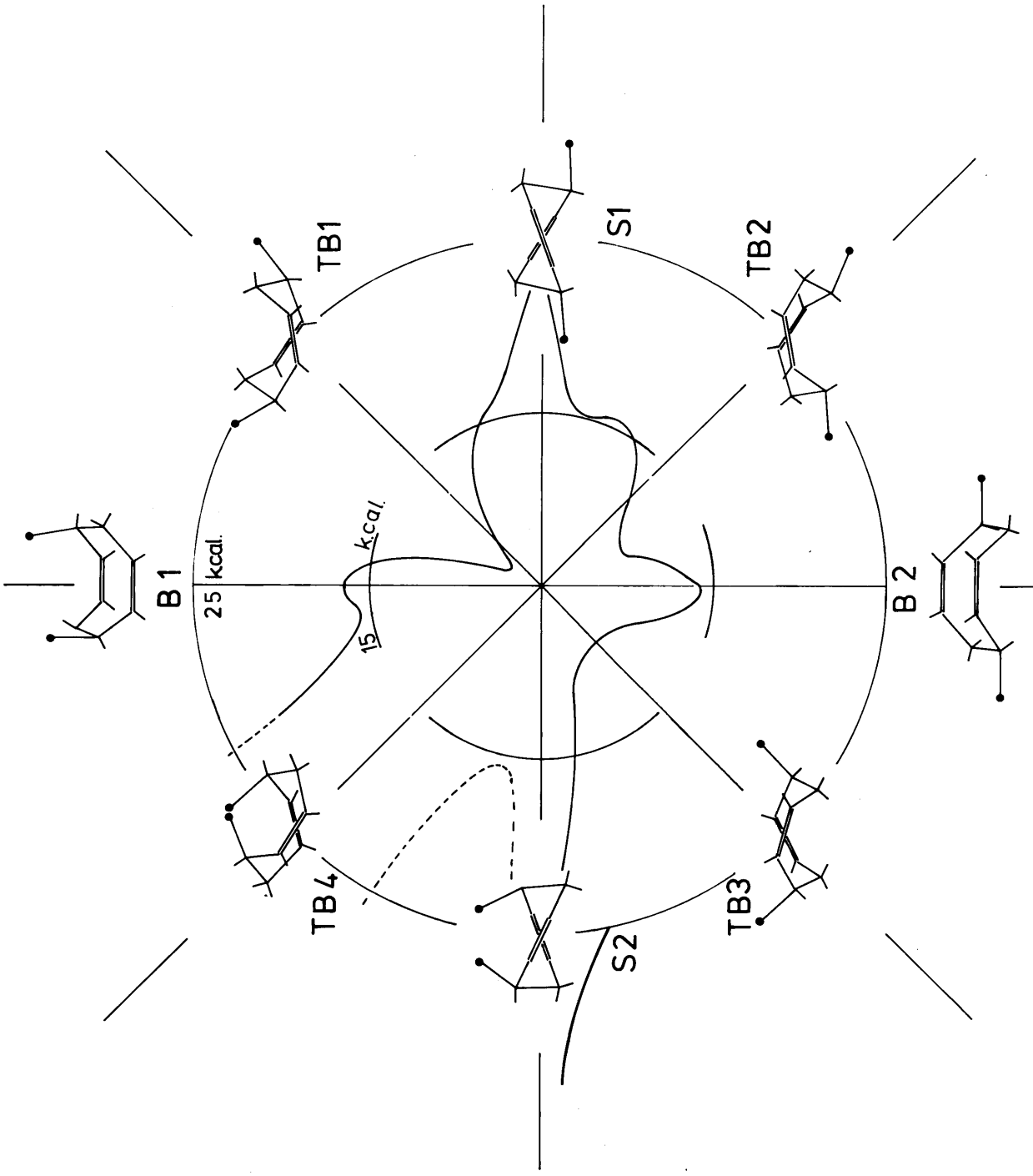

B 1
B 2
TB1
TB2
TB3
TB4
S1
S2
25 kcal.
15 kcal.

TABLE I SDBCOD: COMPARISON OF OBSERVED AND CALCULATED STRUCTURES

PARAMETER	CRYSTAL STRUCT(16)	CALCULATION
BOND LENGTHS (A)		
C(1) - C(2)	1.37(3) *	1.336
C(2) - C(3)	1.48(3) **	1.504 **
C(3) - C(4)	1.51(3)	1.543
BOND ANGLES (DEG.)		
C(1) - C(2) - C(3)	129(2) **	126.1 **
C(2) - C(3) - C(4)	116(2) **	113.5 **
NON-BONDED DISTS (A)		
C(4)...C(8)	3.04 +	3.03
TORSION ANGLES (DEG.)		
C(2)-C(3)-C(4)-C(5)	65 ++	42

* ESDS IN PARENTHESIS
** AVERAGE VALUE
\+ FROM IR SPECTRUM
++ NMR IN SOLUTION ALSO GAVE 65 DEGREES

Fig. 5.3 shows a radial plot of the variation of steric energy with the C(2) - C(3) - C(4) - C(5) torsion angle. The curve has been interpolated (broken line) where necessitated by the inability of the calculation to produce a minimum when severe van der Waals forces are present (e.g. TB4). For reasons noted earlier the relative energies between conformations should be treated with extreme caution particularly in the vicinity of the skew conformations where full relaxation produces a considerable reduction in strain energy by allowing the close-contact transannular atoms (e.g. H3A and H7A for NC) to move further apart. Nevertheless, the results do indicate the existence of three local minima (TB1, TB2 and TB3) which could interconvert and thus support the observation of Mackenzie et al (16) that in solution, at least, more than one twist boat is present. Fig. 5.4 illustrates some of the more probable interconversion pathways and Table II gives the relative energies of the more important intermediates together with the calculated barriers to interconversion.

In view of the uncertainty of the calculations for the boat, skew and TSA and TSB conformations (all of which were not allowed to fully relax) it would be improper to comment further on these conformational barriers.

It is apparent however that the chair form is less stable than twist boats TB1, TB2 and TB3.

1. TB1 → TSA → CHAIR → TSB → TB2

1A. TB1 → TSA → CHAIR → TSB → TB3

2. TB1 → B1 → TB4

3. TB1 → S1 → TB2

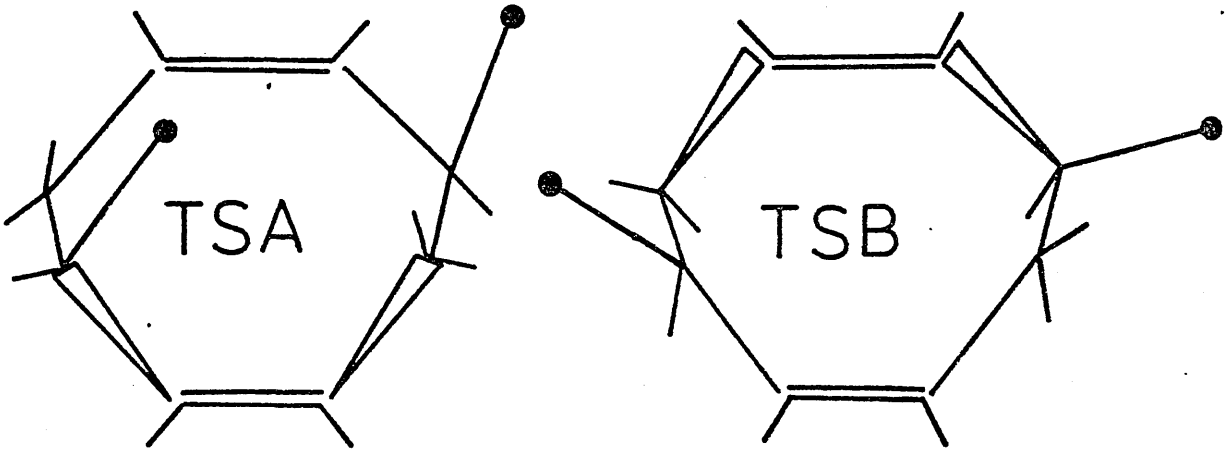


Fig. 5.4 SDBCOD: Pathways for Twist-boat Interconversion.

TABLE II SDBCOD: RELATIVE ENERGIES

CONFORMER	REL. ENERGY *
TB1	0.00
TB3	2.41
TB2	3.05
CHAIR	4.90
TSA	5.21
TSB	6.83
B2	7.97
B1	10.14
S1	18.63
S2	39.25

* ENERGIES IN K.CAL/MOLE

5.4 anti-3,7-Dibromo-cis, cis-cyclo-octa-1,5-diene (ADBCOD)

Results and Discussion

It has, to date, not been possible to isolate this compound (23). Nevertheless, in anticipation of ADBCOD being available at some future date it was decided to investigate its conformational behaviour. MM calculations were carried out as described for SDBCOD and the results are shown in Fig. 5.5 and Table III. All the remarks made with reference to the possibility of only partial maximisation having been achieved for certain conformations of SDBCOD apply equally to ADBCOD.

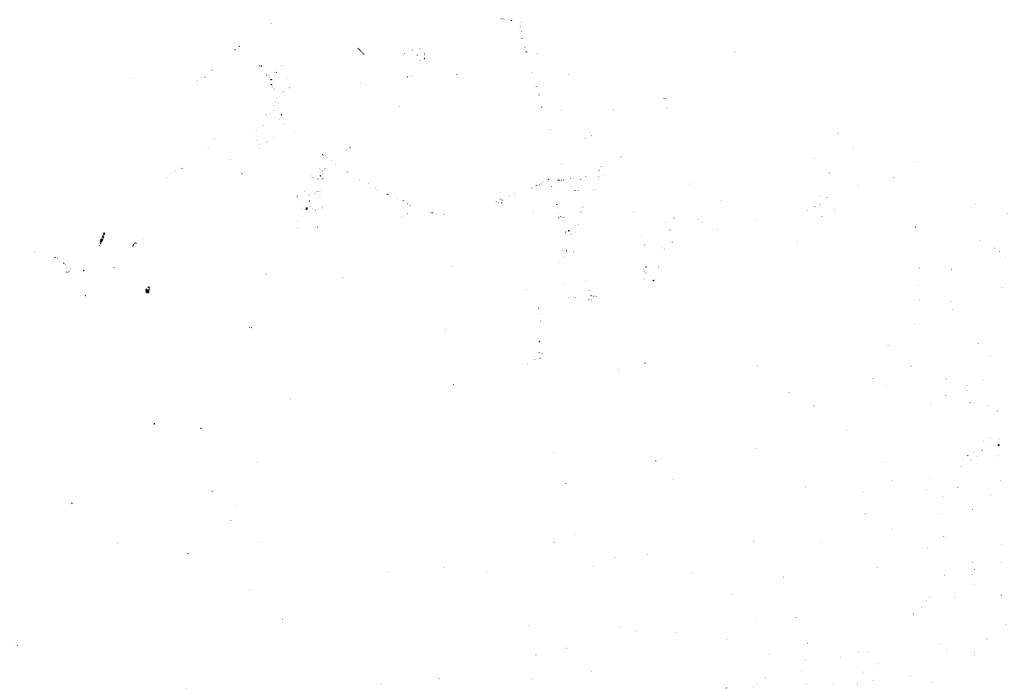
Anti - as opposed to syn - substitution of the bromine atoms at C(3) and C(7) has no symmetry and this results in there being two possible chairs (C and D) in which the bromine atoms can be either diaxial (C) or diequatorial (D). The corresponding boat-to-chair transition states (also called C and D for convenience) either move the bromine atoms closer together (C) or further apart (D) from their relative positions in the boat. Inspection of models indicates that only the following unique conformational changes can occur through the chairs:

$$B1 \rightarrow TSC \rightarrow CHAIR\ C \rightarrow TSC \rightarrow B2$$

$$B1 \rightarrow TSD \rightarrow CHAIR\ D \rightarrow TSD \rightarrow B2$$

The calculations show that there are two isoenergetic global minima (TB1 and TB3) and that the diaxial chair is more stable than the diequatorial variety. This latter result is unexpected and appears to be connected with the

Fig. 5.5 ADBCOD: Variation of energy with conformation



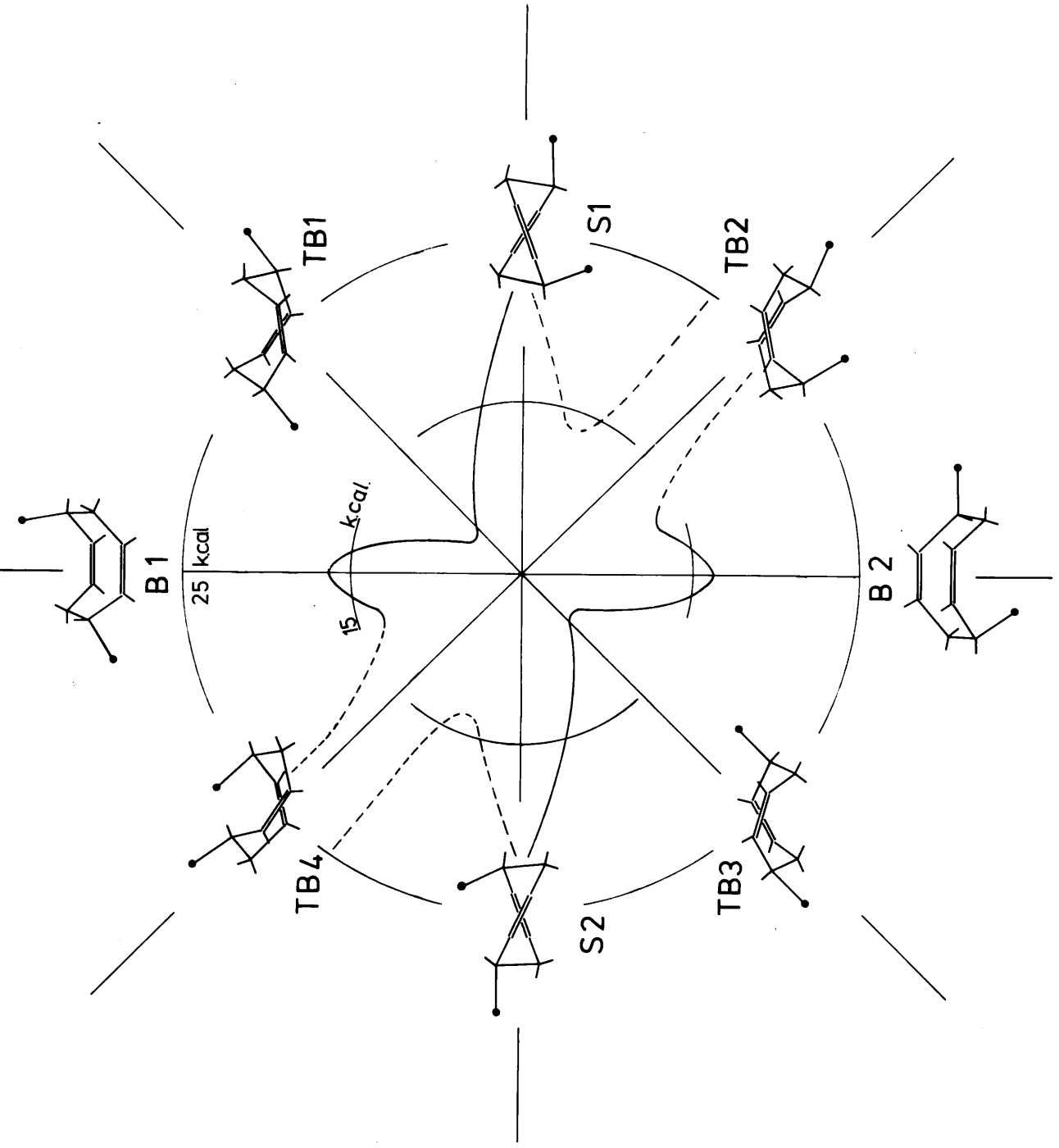

B 1
25 kcal
15 kcal
TB1
S1
TB2
B 2
TB4
S2
TB3

TABLE III ADBCOD: RELATIVE ENERGIES

CONFORMER	REL. ENERGY *
TB1	0.00
CHAIR C	3.34
CHAIR D	4.20
TSC	3.80
TSD	5.49
BOAT	8.53
SKEW	26.42

* ENERGIES IN K.CAL/MOLE

1. TB1 → TSC → CHAIR C → TSC → TB3

1A. TB1 → TSD → CHAIR D → TSD → TB3

2. TB1 → B1 → TB4

3. TB1 → S1 → TB2

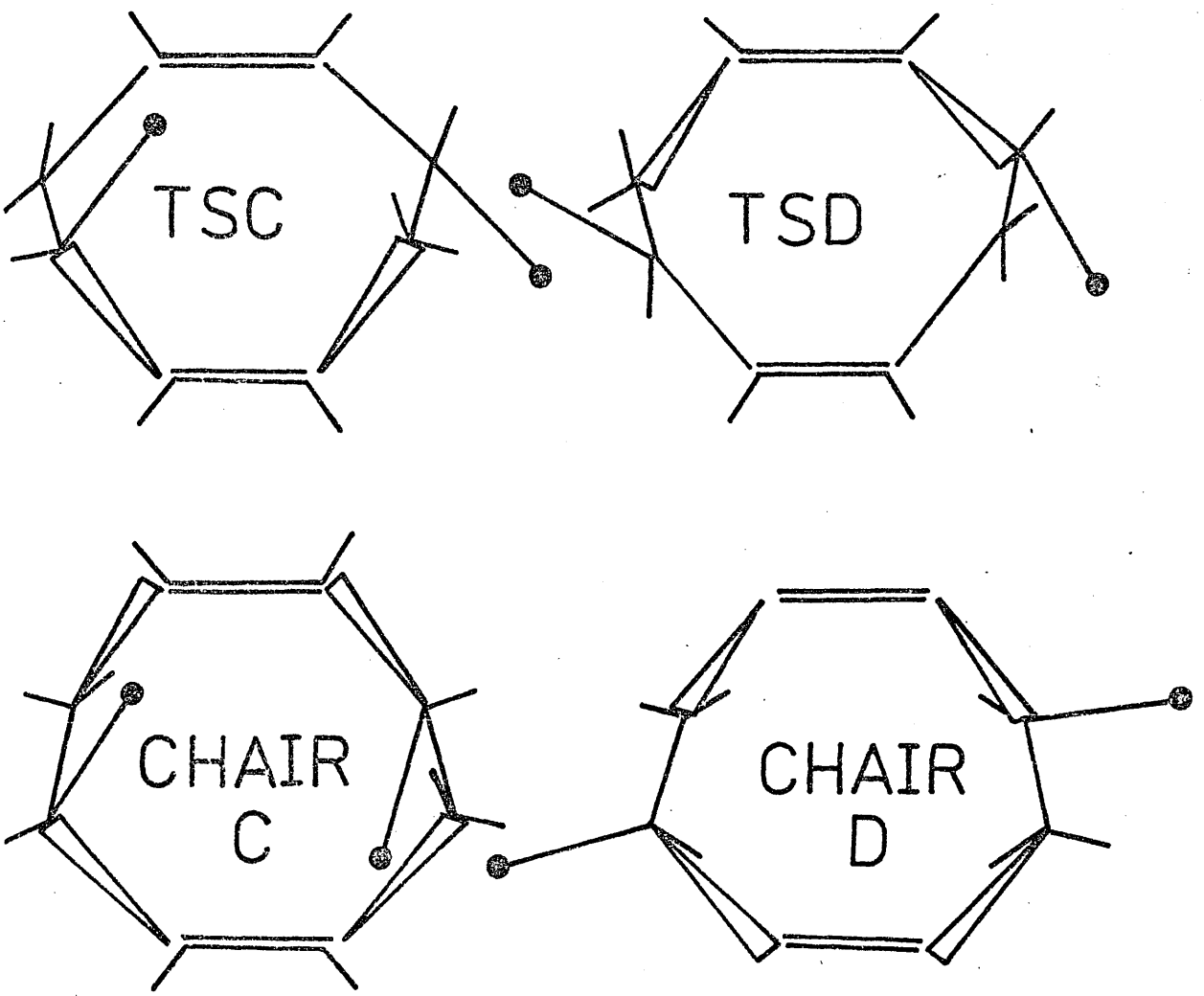


Fig. 5.6 ADBCOD: Pathways for Twist-boat Interconversion.

large van der Waals radius of bromine which in chair D is responsible for substantial non-bonded strain between the bromine atoms at C(3) and C(7) and one of the substituents on the α- carbon atoms.

Once again it is not possible to comment on the barriers for the routes between twist boats (Fig. 5.6).

The relative energies listed in Table III (and Table II) for the constrained boat, skew and TSC and TSD, would almost certainly be reduced under fully relaxed conditions although it is not possible to estimate the relative reduction, and hence the relative stabilities, of each conformer under these conditions.

5.5 cis, cis-Cyclo-octa-1,5-diene (COD)

Introduction

The calculations reported in sections 5.2 and 5.3 served as a preliminary test of the reliability of the FF and facilitated the installation of the suite of computer programs. It was decided to apply this system to the parent hydrocarbon (COD) because both an electron diffraction study (3) and nmr measurements of conformational barriers (4) in COD were available as further tests. Initially FF II was employed to map the pseudorotational circuit and calculate energy differences between key conformations. Subsequently the more extensively parameterised Glasgow alkane/alkene force field (FFI) was used and it is these later calculations that are reported here.

Results and Discussion

The calculated conformation of the twist boat is compared with the geometry observed in the electron diffraction study in Table IV. The agreement is good and the value of the C(2) - C(3) - C(4) - C(5) torsion angle (52°) is close to that of 45° measured in the gas phase (3).* The x-ray analysis of SDBCOD (16) reported the corresponding angle as 65°. Allinger and Sprague (8) and Favini et al (7) have reported angles of 38° and 27° respectively and Ermer, using the Lifson-Ermer FF calculated a value of 55° (30). The uncertainty regarding the electron diffraction result prohibits the use of this angle as an unambiguous test for comparison of the various FFs but the results from FFI and the Lifson-Ermer FF lie somewhere between 45° and 65° and although the connection between an isolated molecule of COD and its crystal syn-3,7-dibromo derivative is tenuous the correlation of the calculated geometry of COD with the electron diffraction results provides evidence of the reliability of FFI.

The calculations support the view that the twist boat geometry represents the steric energy minimum. In the rigid chair, for instance, the torsional strain can only be relieved by an increase in Baeyer strain but in the C_{2V} boat the eclipsing around the C(3) - C(4) and C(7) - C(8) bonds can be reduced by pseudorotation. The decrease in energy arising from the twisting around these bonds is offset by the increasing approach of H4a and H8a (for TB1) and the conformation adopted by the minimum energy boat is directly

* See note (a) Table IV for comments regarding the accuracy of this torsion angle.

TABLE IV COD: COMPARISON OF OBSERVED AND CALCULATED STRUCTURES

PARAMETER	ELECTRON DIFFN(3)	CALCULATION
BOND LENGTHS (A)		
C(1) - C(2)	1.341	1.340
C(2) - C(3)	1.502 *	1.512 *
C(3) - C(4)	1.554	1.530
BOND ANGLES (DEG.)		
C(1) - C(2) - C(3)	127.8 *	127.8 *
C(2) - C(3) - C(4)	116.8 *	115.8 *
NON-BONDED DISTS (A)		
C(1)...C(5)	3.302	3.39
C(1)...C(6)	3.047	3.08
C(2)...C(6)	3.318	3.31
C(3)...C(7)	3.815	3.81
C(4)...C(7)	3.191	3.19
C(4)...C(8)	3.131	3.05
H(4)...H(8)	----	1.94
TORSION ANGLES (DEG.)		
C(2)-C(3)-C(4)-C(5)	45 [a]	52

* AVERAGE VALUE

[a] CALCULATED FROM THE GEOMETRY QUOTED IN REF.3. ASSUMES THAT VALENCE ANGLES C(2)-C(3)-C(4) AND C(3)-C(4)-C(5) ARE EQUAL. THIS IS KNOWN TO BE INCORRECT FROM THE CRYSTAL STRUCTURE OF SDBCOD(16) AND FROM THE CALCULATIONS. THE ELECTRON DIFFRACTION RESULTS THAT ARE AVAILABLE GIVE ONLY AN AVERAGE VALUE FOR THESE ANGLES. HENCE THE ACCURACY OF THE C(2)-C(3)-C(4)-C(5) TORSION ANGLE IS NOT KNOWN.

related to the H.....H non-bonded potentials used in the FF(32). The figures in Table IV indicate that this strain can be relieved by deformation of the ring angles at the sp^2 and sp^3 carbons to 127.8 and 116.8 respectively. The two hydrogens are then moved further apart (calculated separation 1.94A°) while the C(4) and C(8) transannular distance is increased from ca. 2.3A°, apparent from an undistorted Dreiding model, to 3.131A° reported in the electron diffraction study. The calculated value is 3.05A° and the x-ray analysis of SDBCOD(16) gave this distance as 3.04A°.

The balance achieved in the minimum energy boat is changed if the pseudorotation is continued towards the skew form since there is an increase in the Pitzer strain around C(3) - C(4) and C(7) - C(8), and in the skew form itself there are two pairs of hydrogens (H4a, H8a; and H3a, H7a) in close contact. The need for extreme caution when calculating the strain energy of intermediates such as the skew has been discussed from the symmetry view point in section 5.2. In purely mechanical terms, full relaxation permits co-operative movements of the atoms and the illustrations of the geometry of the non-constrained (NC) and fully constrained (C) skew conformations of COD show that this results in a reduction of the H...H transannular repulsions. Inspection of the calculated structures indicates that this is achieved by a flattening of the ring.*

The calculation has thus been very successful in

*The energy calculated for the constrained molecule is correct for <u>that molecule</u> but this structure is not a major intermediate on the pseudorotational pathway because a substantial reduction in strain energy is achieved by adoption of the NC geometry.

reproducing the geometry of the twist boat and for COD there are four of these (isoenergetic) twist boats on the pseudorotational circuit. Only one quadrant of this circuit is unique but because each twist boat has a different pair of methylene hydrogens in close contact it is possible, by use of the low temperature nmr technique, to observe and measure any interconversion of twist boats which might be taking place. This is precisely what has been done by Anet and Kozerski (4) and their spectra are shown in Fig. 5.7. The ^{13}C nmr spectra for the methylene carbon resonance changes from a single peak at high temperatures to a 1:1 doublet at -176°. The symmetries of the boat, chair, and skew forms are such that methylene carbons are always equivalent and therefore the doublet at -178° must represent a twist boat (the methylene carbons in the boat to chair 6 co-planar transition state are also non-equivalent but because this is more unstable than either the boat or the chair it would not be observed as a single entity). The singlet at high temperatures is therefore consistent with rapid interconversion of twist boats (process A, with $\Delta G = 4.2 \pm 0.2$ K. cal mole^{-1} at -176°) resulting in each of the methylene carbon pairs (C(3), C(7) and C(4), C(8)) interchanging steric environments.

The possible pathways for such interconversion are given in Figure 5.8 and the pmr spectra of the methylene protons show that two of these conversion processes are occurring simultaneously (at room temperature), one with a $\Delta G = 4.4 \pm 0.1$ K. cal mole^{-1} at -177°(process B) and the other with $\Delta G = 4.9 \pm 0.1$ K. cal mole^{-1} at -168°(process C).

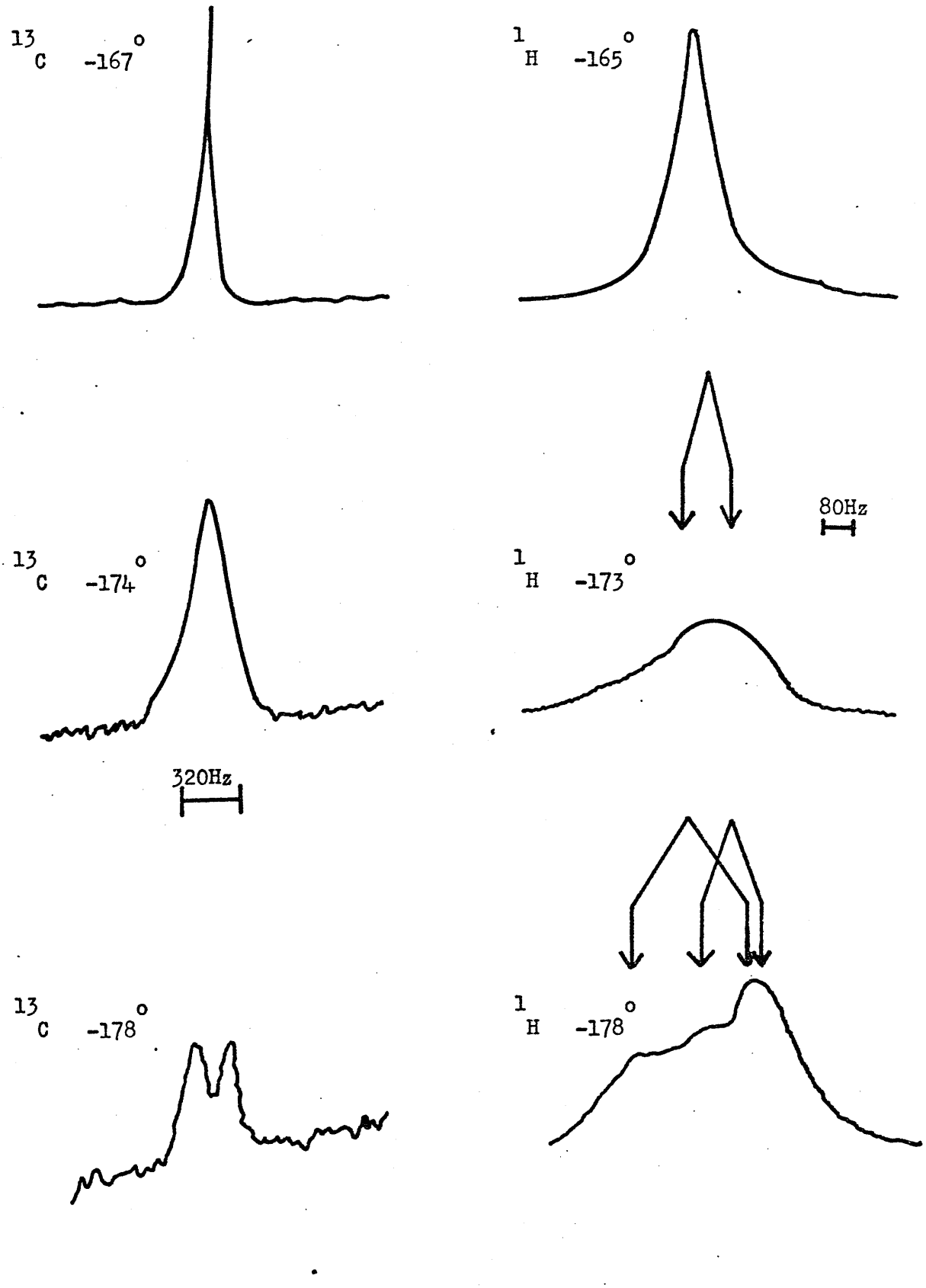


Fig. 5.7 COD: Variable Temperature NMR Spectra of Methylene Groups(4)

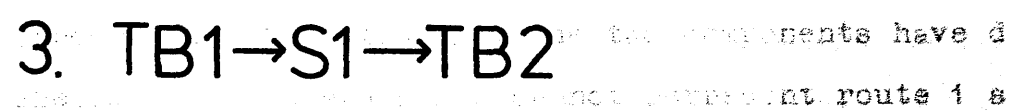


Fig. 5.8 COD: Pathways for Twist-boat Interconversion.

The assignment* of the three spectral processes:

A	$\Delta G = 4.2$ K cal mole^{-1} at $-176^{\circ}C$
B	$\Delta G = 4.4$ K cal mole^{-1} at $-177^{\circ}C$
C	$\Delta G = 4.9$ K cal mole^{-1} at $-168^{\circ}C$

to specific modes of twist boat interconversion:

1	TB1 $\rightarrow$ B1 $\rightarrow$ CHAIR $\rightarrow$ B2 $\rightarrow$ TB
2	TB1 $\rightarrow$ B1 $\rightarrow$ TB4
3	TB1 $\rightarrow$ S1 $\rightarrow$ TB2

is not unambiguous. However, the ^{1}H spectrum at $-177^{\circ}C$ (process B) indicates that the two components have different chemical shifts and hence cannot represent route 1 since there are two possible chairs (the one formed being determined by which group of 6 atoms is coplanar in the transition state) leading to complete averaging.

The following possibilities therefore exist:

Process B represents Route 2

and

Process C represents Route 1 or Route 3

OR

Process B represents Route 3

and

Process C represents Route 1 or Route 2

Process A observed in the ^{13}C spectrum must involve the sum of processes B and C. In their report Anet and Kozerski state that the path representing process 2 "can in principle be determined ... by accurate strain energy

*e.g. Process A is not necessarily assigned to route 1.

calculations".

These workers have now carried out such calculations and their results, together with those from other sources (7, 8, 30), are shown in Table V. There is broad agreement between the predictions of Ermer (30), Anet and Kozerski, and this work regarding the relative order of the conformational barriers. The calculations of Favini et al (7) were only concerned with computing the energies of various isolated conformers of COD and therefore cannot be applied to this discussion. Allinger and Sprague (8) find the skew as the most unstable conformation; an identical result to that obtained by the author for the fully constrained model, thus suggesting that they have not allowed co-operative movements of the atoms.

The calculations reported in this thesis indicate that:

Process B represents route 3 (skew)

Process C represents route 2 (boat)*

As noted previously there are discrepancies between the observed and calculated barriers and these are of about the same order as those found by other workers.

In the following discussion the nmr spectra are explained in terms of these assignments.

*The energy difference between routes 1 and 2 is only 0.1 K.cal and therefore this assignment is not unambiguous. However, both Ermer, and Anet and Kozerski also find route 2 to be preferred to route 1 (and Ermer obtains a difference of 0.2 K.cal between them, in the same sense).

TABLE V COD: RELATIVE ENERGIES FROM VARIOUS SOURCES

CONFORMER	RELATIVE ENERGY *				
	FAVINI(7)	ALLINGER(8)	ANET(31)	ERMER(30)	THIS WORK
TB	0.00	0.00	0.00	0.00	0.00
CHAIR	2.75	1.45	---	---	0.77
BOAT	3.84	3.05	---	---	4.55
SKEW	6.44	5.94	---	---	2.27
TRANSITION STATE	---	5.23	---	---	4.64
ROUTE 1	---	5.23	7.2	5.91	4.64
ROUTE 2	3.84	3.05	6.6	5.73	4.55
ROUTE 3	6.44	5.94	4.2	4.15	2.27

MEASURED BARRIERS BY NMR(4)

	BARRIER	POSSIBLE COMBINATIONS OF ROUTES	
PROCESS B	4.4 *	ROUTE 2	ROUTE 3
PROCESS C	4.9 *	ROUTE 1 OR ROUTE 3	ROUTE 1 OR ROUTE 2

* ENERGIES IN K.CAL/MOLE

The ^{13}C spectrum results from the simultaneous occurrence of (1) TB1 to TB2 conversion (Fig. 5.7) through the skew and (2) TB1 to TB4 via the boat taking place less frequently.* This spectrum of the methylene carbons gives only their interchange in environment resulting from twist boat interconversion since the symmetries of the intermediate skew and boat prevent their conformations being observed in ^{13}C spectroscopy. The pmr spectrum, however, distinguishes between the two pathways. The methylene proton band at $-165^{\circ}C$ is composed of a single peak because at that temperature it is possible to interconvert between all four twist boats and so on average each of the eight methylene protons can occupy all the possible steric environments. The calculations have indicated that lowering the temperature to $-173^{\circ}C$ prevents the route 2 process from taking place. This produces the doublet observed since four of the methylene protons are always "outside" (in the sense that they cannot come into close contact as H4a and H8a in TB1) while the other four are always "inside". Thus this rocking motion via the skew between TB1 and TB2 which is still taking place at $-173^{\circ}C$ averages the shifts of the "inside" protons and also averages the "outside protons" giving the observed spectrum. The activation energy for this process is too high to be overcome at $-178^{\circ}C$ and the ^{1}H spectrum at this temperature is given by the four different types of methylene proton present in an isolated twist boat.

*Strictly, all three processes are occurring but for simplicity the discussion has been restricted to the two major interconversions.

5.6 anti-3,7-Dimethyl-cyclo-octa-1,5-diene (ADMCOD)

Introduction

The results for COD show that FFI is able to reproduce the energies and geometries of its various conformational possibilities. As stated previously, FFI cannot at present be used for strain energy calculations on SDBCOD and ADBCOD because it has not been parameterised for the bromine interactions. The lack of experimental data for ADBCOD (see section 5.4) prevented the predictions for that compound being tested. However, the recent synthesis of ADMCOD (22) and the co-operation of Professor Heimbach in supplying a sample for nmr analysis provided an opportunity for further study of both the reliability of FFI and of the conformational situation in anti-3,7-derivatives of COD.

Results and discussion

The full nmr results are not yet available because of equipment problems but preliminary spectra indicate that there is just one main interconversion process occurring with a barrier of about 5 K.cal per mole (23).

Some of the possible processes are shown in Fig. 5.9 and the calculated relative energies of the major conformers are listed in Table VI. The conformational variety possible in ADMCOD is exactly as described previously for ADBCOD. Thus the relationship of the transition states and chairs to each other and to the diequatorial or diaxial location of the bromine atoms of ADBCOD remains unaltered on the anti- substitution of the methyl groups.

In ADMCOD utilisation of the full matrix relaxation technique has shown that TB2, TB4, the boat (of approximate C_{2v} symmetry), and the skew are all local stationary points (either maxima or inflexions) and the present calculations give little indication of the form of the energy vs. reaction coordinate curve between them. Fortunately route 1A through the diequatorial chair (D) represents the minimum energy route

1. TB1 → TSC → CHAIR C → TSC → TB3

1A. TB1 → TSD → CHAIR D → TSD → TB3

2. TB1 → B1 → TB4 → S2 → TB3

3. TB1 → S1 → TB2 → B2 → TB3

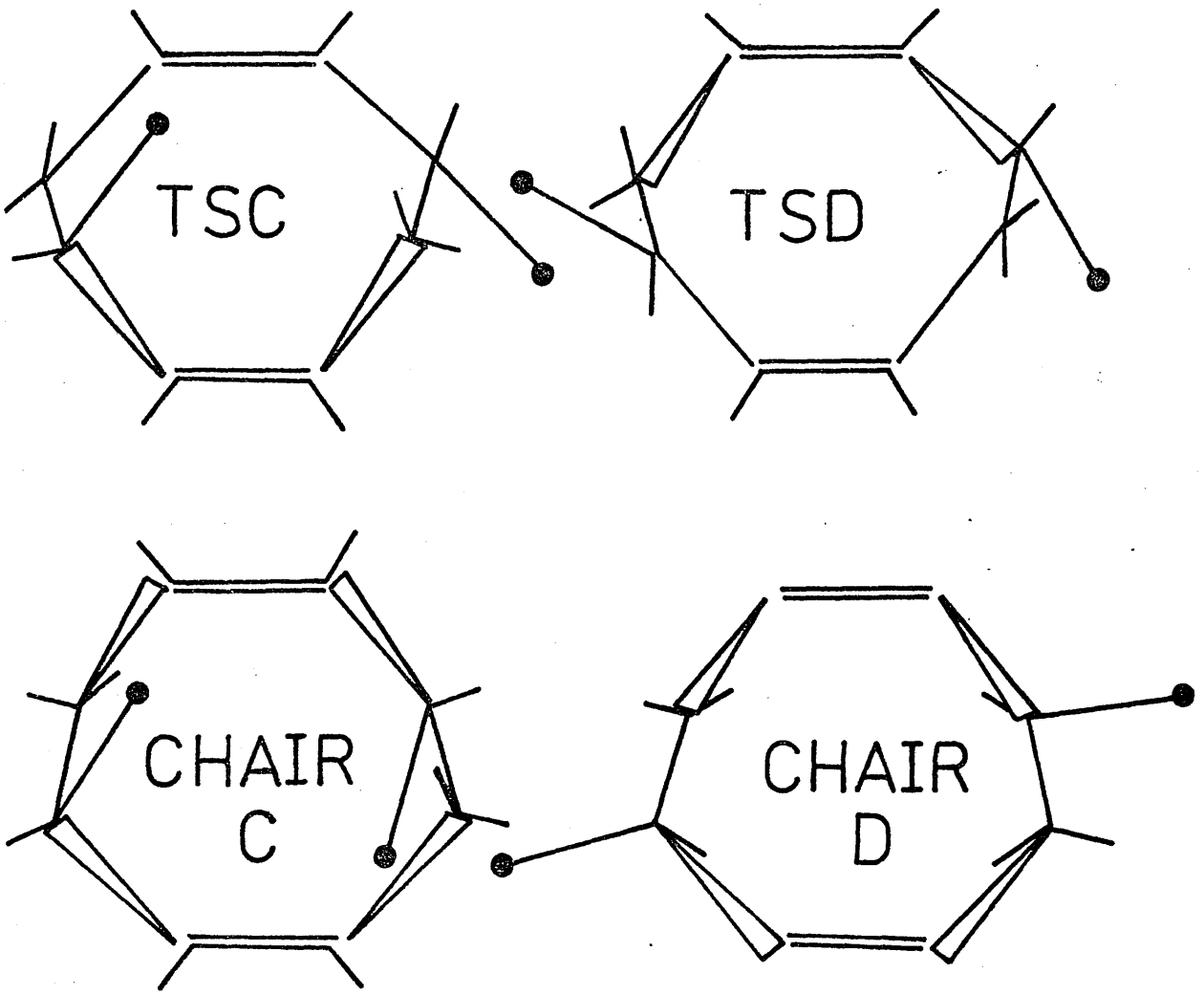


Fig. 5.9 ADMCOD: Pathways for twist-boat interconversion

TABLE VI ADMCOD: RELATIVE ENERGIES

CONFORMER	REL. ENERGY *
TB1	0.00
CHAIR D	0.95
CHAIR C	2.26
TSD	4.98
TSC	9.02
TB2/TB4	6.61
BOAT	5.78
SKEW	13.03

ROUTE 1	9.02	(THROUGH CHAIR C)
ROUTE 1A	4.98	(THROUGH CHAIR D)
ROUTE 2	6.61	(THROUGH BOAT AND TB4)
ROUTE 3	13.03	(THROUGH SKEW AND TB2)

* ENERGIES IN K.CAL/MOLE

and this is therefore indicated as the main process observed in the low temperature nmr. It is not clear however whether the approximate $\underline{C}_{2V}$ boat is a necessary precursor of the chair*.

Inspection of Dreiding models has suggested that the 6-coplanar transition state** of Roberts can be formed from a member of the boat family in which the C(2)-C(3)-C(4)-C(5) torsion angle is 10 or even 20° and more evidence is required before this anomaly can be resolved. It would be particularly interesting to have some information on the processes taking place (and the barriers to them) in more sterically crowded 3,7-anti-substituted octadienes which should have a larger energy differential between the boat and TSD.

* Anet (ref. 30 p571) has remarked that the lowest barrier for an interconversion process might only be reached in some cases by driving several torsion angles simultaneously and unsymetrically.

**See section 5.7 for further discussion of the exact conformation of the transition state.

5.7 Comparison of results

The employment of two different FFs for the calculations on COD and its 3,7 disubstituted derivatives restricts the degree to which comparisons can be made. The improvements in the more recent of the two FFs (FFI) may be expected to affect the proportion of the total strain arising from each type of contributor rather than the relative order of the various conformers. The initial calculations for COD and ADMCOD were carried out with FFII so that results are available from both FFs for these two compounds and reinforce the previous statement. The discussion which follows is nevertheless not detailed because it is based on calculations performed with both FFI (COD and ADMCOD) and FFII (SDBCOD and ADBCOD).

The minimum energy conformation is the twist boat for all four compounds although the value of the C(2) - C(3) - C(4) - C(5) torsion angle varies between 42° and 52°. This is not altogether unexpected since this angle is dependant on the magnitude of H... H interaction in the FF used (32) and also the precise effects of (i) the differences between the environments in which the observed values of 45° and 65° were measured and (ii) the substitution in the series, are not known.

The calculated C(4) .... C(8) separations and the endocyclic angle deformation are consistent with the experimental geometries (3, 16).

Substitution of the anti methyl groups at C(3) and

C(7) has little effect on the relative stabilities of most of the conformers encountered. It does, however, change the major intermediate for twist boat interconversion from the skew (COD) to the diequatorial chair (ADMCOD) because of the strain imposed on the TB2 and TB4 forms of ADMCOD.

Both the boat intermediate and TB4 are, in the case of ADMCOD, distorted conformations of the 'purer' forms obtained for COD, and this is a reflection of the extra strain imposed on the molecule by the methyl substitution.

The boat to chair transition state proposed by Roberts does not have six atoms in one plane for either COD or ADMCOD. Unconstrained full matrix minimisation has indicated that these six atoms, C(3) to C(8), have a maximum of four atoms lying in one plane, the other two atoms being displaced slightly from this plane. This situation is very similar to that suggested by Ermer (26) for cyclohexane.

The relative stabilities of the chair conformations of ADBCOD and ADMCOD requires comment. It was noted in Section 5.4 that the diaxial chair was preferred for ADBCOD, and this was explained on the basis of the non-bonded strain between the bromines and one of the α -hydrogen atoms in the diequatorial chair. In ADMCOD this latter chair is more stable since the methyl substitution changes the contact distances and can also reduce these interactions by rotation about the C(3) - and C(7)-methyl bonds. The diaxial chair of ADMCOD has more van der Waals strain than

the corresponding conformer of ADBCOD as a result of the increased number of additional atoms ($-CH_3$ as opposed to -Br) and their greater proximity to the octadiene ring.

The general agreement between the various FFs in interpreting the spectra for COD is encouraging, although the calculated barriers are not as close to the measured values as might be desired. Nevertheless, with the exception of Allinger's calculations,* the other independant studies of COD (26,31) find the same relative order of preference for the three pathways as reported here and enable some confidence to be placed in the predictions made by FFI for ADMCOD.

*The reasons for this have been discussed in Sections 5.2 and 5.5.

5.8 References

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CHAPTER SIX

Studies of germacranolide stereochemistry

6.1 Introduction

The considerable body of experimental data available on the stereochemistry of sesquiterpenes (e.g. 1,2,3) has revealed several phenomena of which only a small number have been interpreted.

The work reported in this chapter was carried out in order to investigate certain of the observed peculiarities of germacranolides. In particular some aspects of the stereochemistry of those germacranolides possessing an α-methylene (or methyl) -γ- lactone fused to a trans, trans,-cyclodeca-1,5 diene ring (Fig. 6.1) have been put on a quantitative basis by the application of molecular mechanics (MM).

The macrocycle in these systems is known to occur frequently in two of the possible conformations of trans, trans,-cyclodeca-1,5,diene (I). Conformation A (Fig. 6.2) has been observed in, for example, costunolide (4), elephantol (5) and alatolide (6) while conformation B is typified by dihydromikanolide (7) and shiromodiol (8) but, apart from some preliminary calculations by Favini (9), very little is known about the relative stabilities of the various conformations of I. In addition the trans, trans-double bonds are deformed by consistently different amounts from the ideal value of 180° for the C—C=C—C torsion angles (10) and the data currently available are insufficient to show whether this is caused by the substitution of the lactone ring and/or the other substituents to I, or

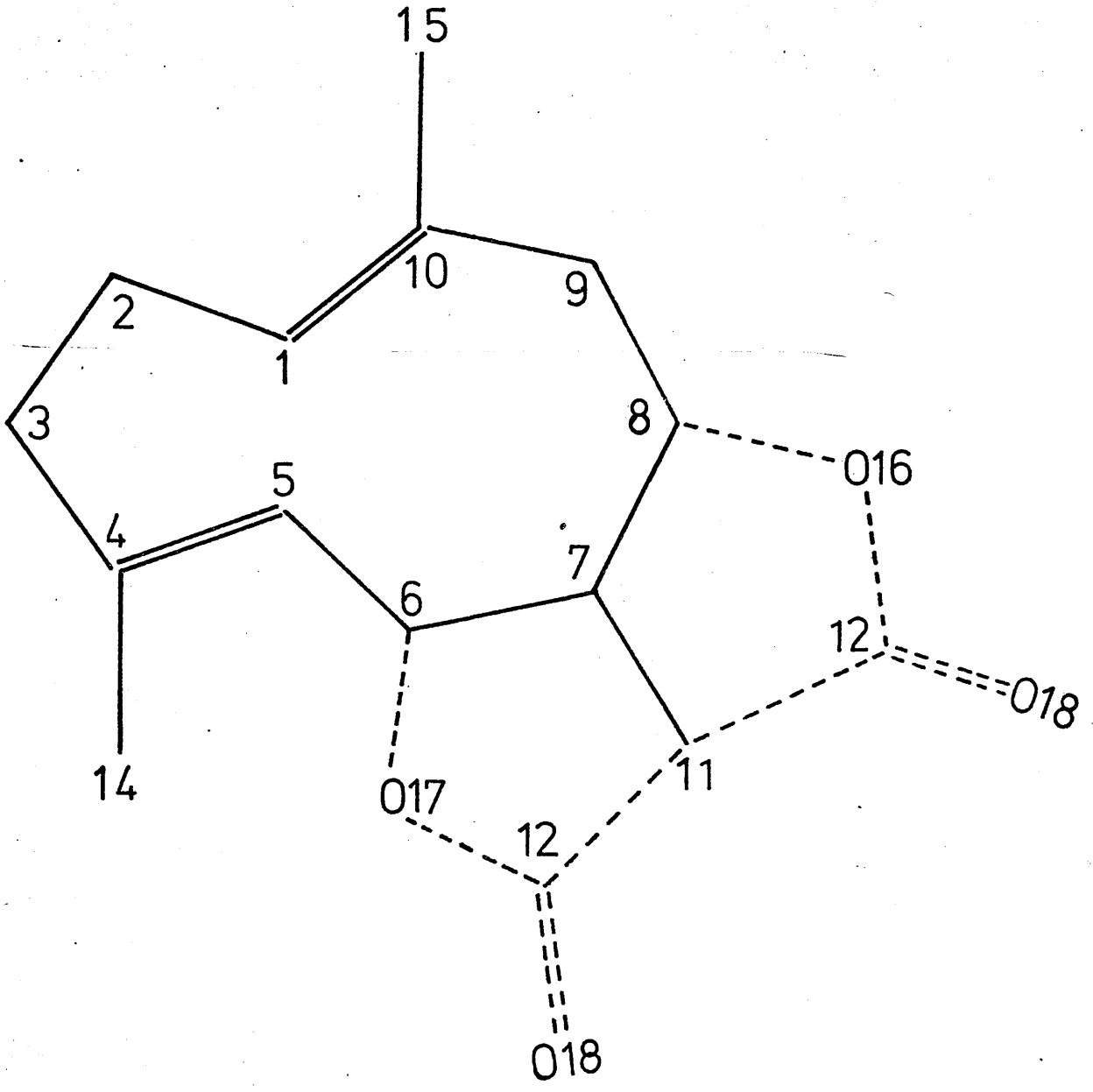
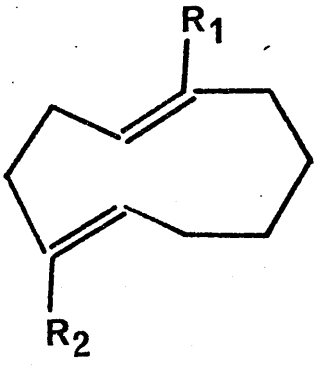
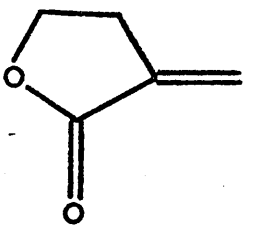


Fig. 6.1 Basic Structure of Germacrane Sesquiterpene γ-Lactones

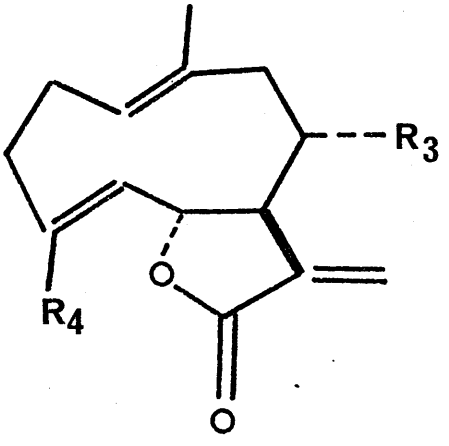


I $R_1 = R_2 = H$

X $R_1 = R_2 = Me$



XIV



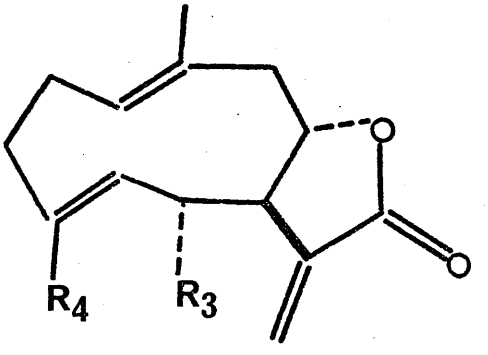
II $R_3 = OH$, $R_4 = CH_2OH$

III $R_3 = OCOCCH(OH)CH_2OH$, (CH_2 = CH_2)

$R_4 = CH_2OH$

IX $R_3 = H$, $R_4 = Me$

XII $R_3 = OH$, $R_4 = Me$



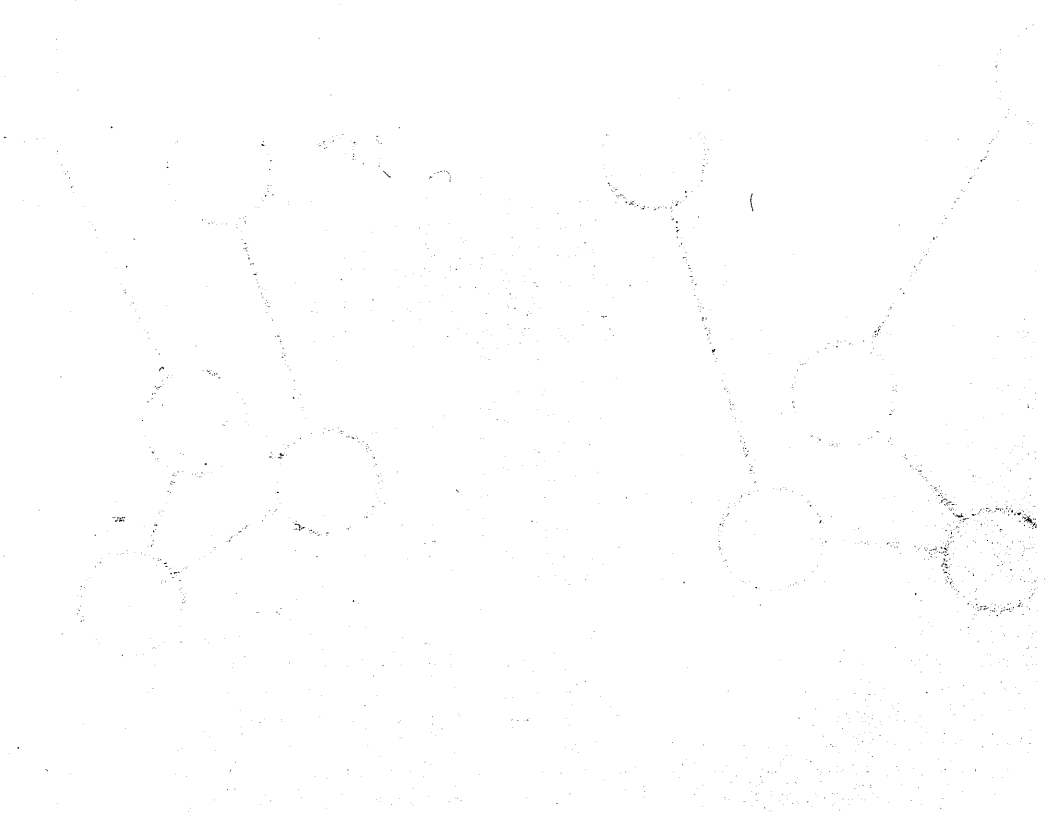
IV $R_3 = OH$, $R_4 = CH_2OH$

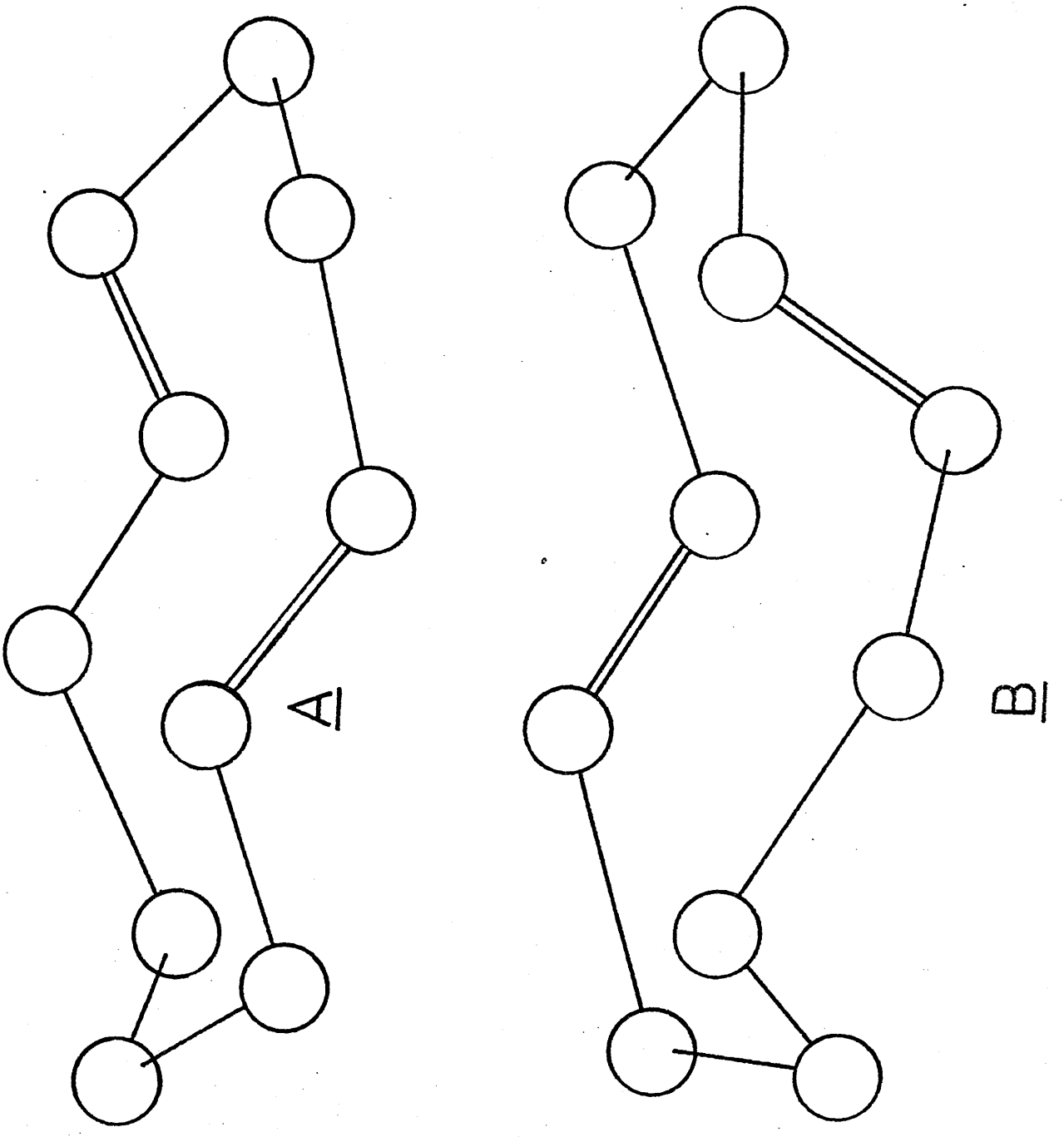
XI $R_3 = H$, $R_4 = Me$

XIII $R_3 = OH$, $R_4 = Me$

Fig. 6.2

The A and B type conformations of cyclodeca-1,5-diene




A1
B1

whether it is a feature of the isolated cyclodecadiene.

The location and conformation of the lactone ring poses further questions. Several workers, for instance, noticed that the lactone function was capable of taking part in a rearrangement process in which it could change its fusion from C(6), C(7)— to C(7), C(8)— (Fig. 6.1) (e.g. 11,12). Yoshioka et al (13) on further investigation of trans - fused germacranolides which contain C(6)- and C(8)- lactonisable α-orientated oxygen substitution found that they preferentially relactonise at C(8) after treatment with strong alkali and subsequent acidification. Thus salonitenolide (II) and cnicin (III), for example, form artemisiifolin (IV). The complexity of interatomic forces involved in determining the relative stabilities of the C(6), C(7)— and C(7), C(8)— modes of fusion can only be unambigously rationalised by a quantitative method such as reliable strain energy calculations.

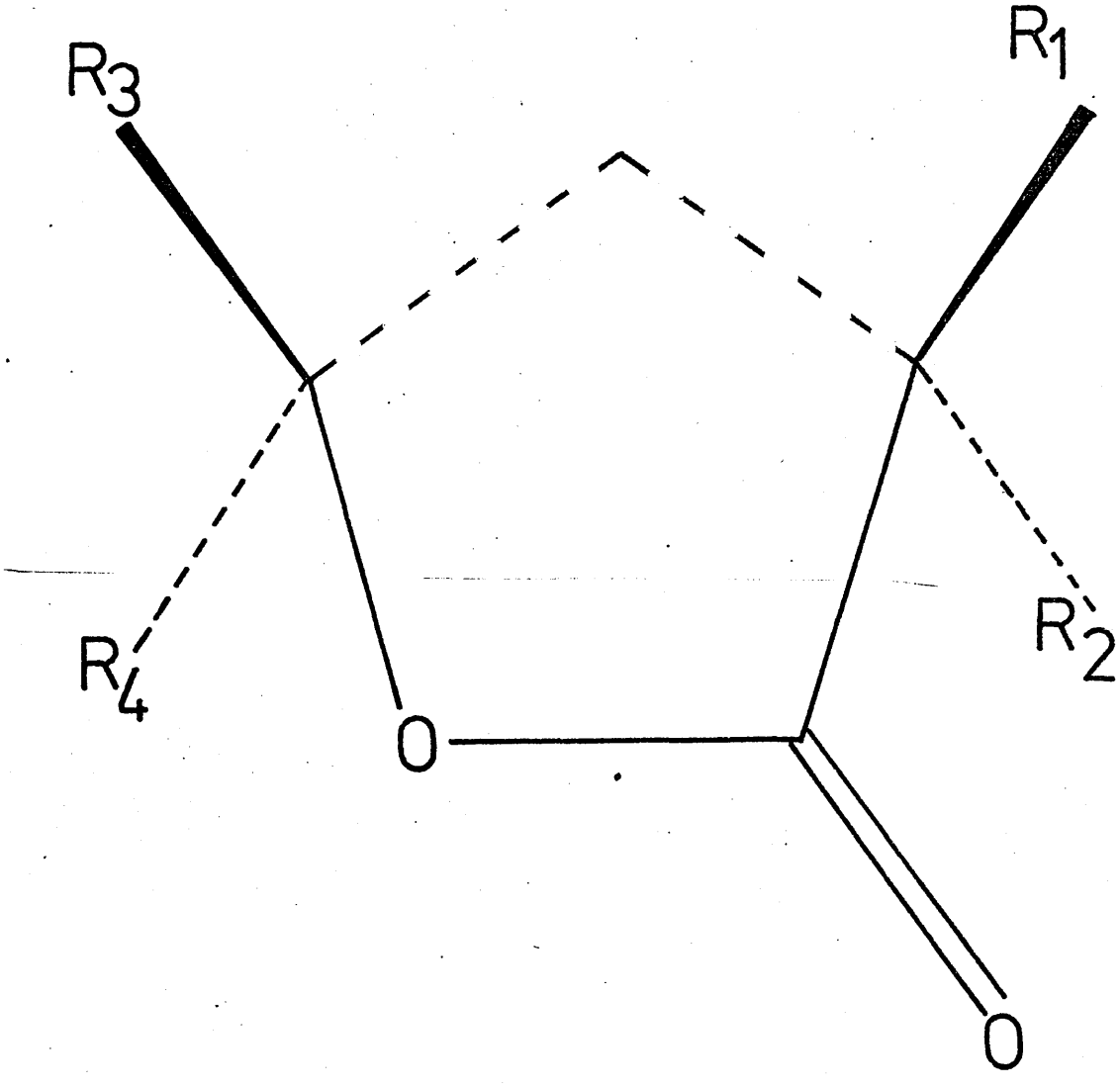
The lactone fusion in germacranolides has been correlated with the Cotton effect at about 250 nm by Beecham (14) who proposed that the sign of this spectrum is related to the chirality of the **C=C-C=O** chromophore. McPhail and Sim (6), however, have noted the apparent insensitivity of the Cotton effect to changes in the **C=C-C=O** torsion angle (Ψ) and have suggested that the torsion angle (Φ) in the vicinity of ring fusion may be more significant. It has also been shown that the value of Ψ can sometimes be significant in determining the relative stabilities of isomeric sesquiterpenes such as α-and β-santonin (16).

The correlation (if any) between $\underline{\Psi}$ and $\underline{\Phi}$ is not immediately obvious and again this is the type of problem which MM should be able to answer. The MM technique has also been used to investigate the relationship between $\underline{\Psi}$ and steric strain in germacranolides.

6.2 Method of calculation

One of the difficulties in using MM to study the problems discussed in section 6.1 is parameterisation of the lactone terms in the force field (FF). The paucity of experimental data for lactones is evident from the inclusion of only one lactone $\Delta H^{o}_{f}(g)$ in Cox and Pilcher (18) and a complete absence of electron diffraction results for lactones in Specialist Periodical Reports (19). The force field (FFIII, appendix C) had therefore to be constructed on an _ad hoc_ basis. Fortunately, most of the required terms were already available in an FF which had proved successful in reproducing and interpreting the observed stabilities of several isomers of the santonin family (16). The alkane, alkene, and carbonyl interactions in this FF were taken from Allinger's FF (20,21) because the Glasgow alkane/alkene FF(22) had not been fully parameterised when the calculations were carried out. Allinger's FF has been tested against experimental data for a number of compounds including some steroids (23,24).

FF III, while not being suitable for predicting the absolute strain energies in unrelated compounds should, nevertheless, be adequate for calculating the relative enthalpies of compounds that are structurally similar (25). In order to further test this assertion the FF was applied to the results of some recent equilibration studies on 2,4- disubstituted - γ -butyrolactones (26). These observations yielded the free-energy differences between the cis — and trans isomers of V - VIII and since the entropy differences within each group of geometric isomers are probably very small it is permissible to equate calculated variation in enthalpy with observed free energy. The cis II isomers of V - VIII were not included in the calculations because they are very highly strained as a result of a number of transannular interactions and consequently do not make a significant contribution to the equilibria. Strain energies were computed for the trans I and II and cis I conformers of these compounds employing FF III and full matrix minimisation. The results are shown in Table I and because similar energies were obtained for the two trans forms of each compound it was necessary to take a weighted average based on their calculated Boltzmann distribution. The agreement between the calculated and observed results is very good, particularly in view of the relatively small spread in ΔG. The authors of the report on the equilibration studies expressed the view that the cis isomers were more stable because, although the minimum energy form for both cis and trans structures was an envelope in which the endocyclic C-C(=O)-O-C



COMPOUND	TRANS I	TRANS II	CIS I	CIS II
	$R_1=R_4=H$	$R_2=R_3=H$	$R_1=R_3=H$	$R_2=R_4=H$
	R_2 R_3	R_1 R_4	R_2 R_4	R_1 R_3
V	Me Me	Me Me	Me Me	Me Me
VI	Et Me	Et Me	Et Me	Et Me
VII	Bu^t Bu^t	Bu^t Bu^t	Bu^t Bu^t	Bu^t Bu^t
VIII	Bu^n Me	Bu^n Me	Bu^n Me	Bu^n Me

TABLE I STABILITIES OF 2,4-DISUBSTITUTED-γ-BUTYROLACIONES

COMPOUND	ENERGY *		RATIO **	ENERGY *		DELTA G *	
	TRANS I	TRANS II	TII / TI	TRANS $	CIS I	CALC.+	OBSV.++
V	2.56	2.99	0.49	2.70	2.39	-0.31	-0.14
VI	2.68	2.82	0.79	2.74	2.50	-0.24	0.00
VII	-0.27	-0.05	0.70	-0.18	-1.21	-1.03	-1.20
VIII	2.06	2.23	0.74	2.13	1.86	-0.27	-0.19

* K.CAL/MOLE

** BOLTZMANN DISTRIBUTION OF ISOMERS AT 298K

$ WEIGHTED MEAN OF TRANS ENTHALPIES USING RATIO TII / TI

\+ DIFFERENCE (CIS I - MEAN OF TRANS)

++ FROM REF.26. DELTA G AT 298K

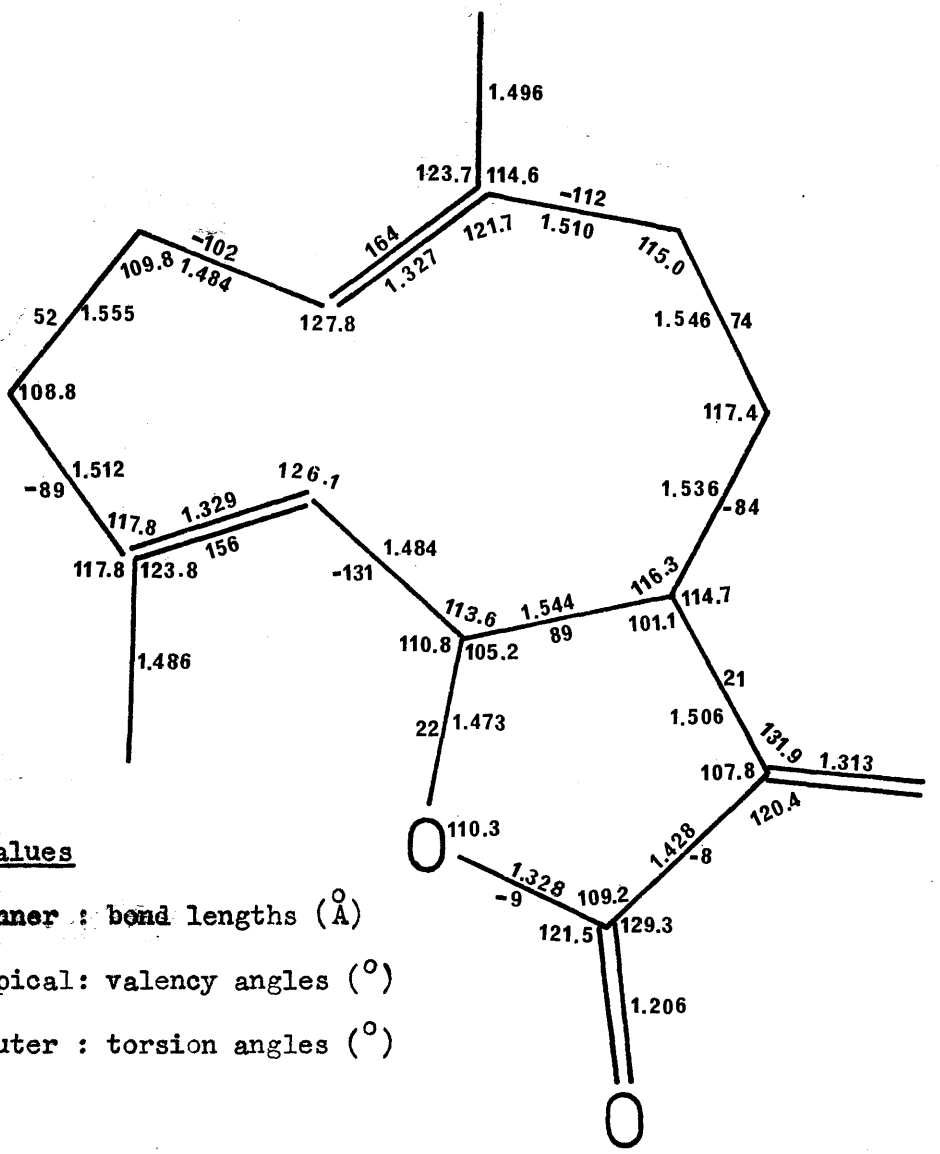
torsion angle was 0°, the cis alkyl (or aryl) substituents were quasi-equatorial, whereas in the trans isomers one of these substituents must be quasi-axial. The calculations fully support this view.

The reliability of FF III is reinforced by its ability to reproduce the geometry of costunolide (IX). The observed (4) and calculated structures of IX are shown in Figs. 6.3 and 6.4 respectively. The root-mean-square (r.m.s.) differences in bond lengths, bond angles and torsion angles between the two determinations are $0.013A^{\circ}$, 2.0° and 5° respectively. The corresponding estimated standard deviations in the x-ray study are $0.003A^{\circ}$, 0.2° and 0.3°.

The calculations on the butyrolactones and on IX when considered in conjunction with the results reported for the santonins vindicate the use of this FF for investigation of the problems outlined in section 6.1.

6.3 Conformation of the trans, trans - cyclodeca - 1,5 - diene (I)

The frequent occurrence of two of the possible conformations of I in germacranolides was noted in section 6.1. Calculations were carried out on these A and B conformers (Fig. 6.2) using both FF III and the recently parameterised FF I (27). The results from these two independant FFs, together with the measured torsion angles for costunolide (4), are shown in Fig. 6.5.



Values

Inner : bond lengths (Å)

Apical: valency angles (°)

Outer : torsion angles (°)

Fig. 6.3 Costunolide: Crystal Structure.

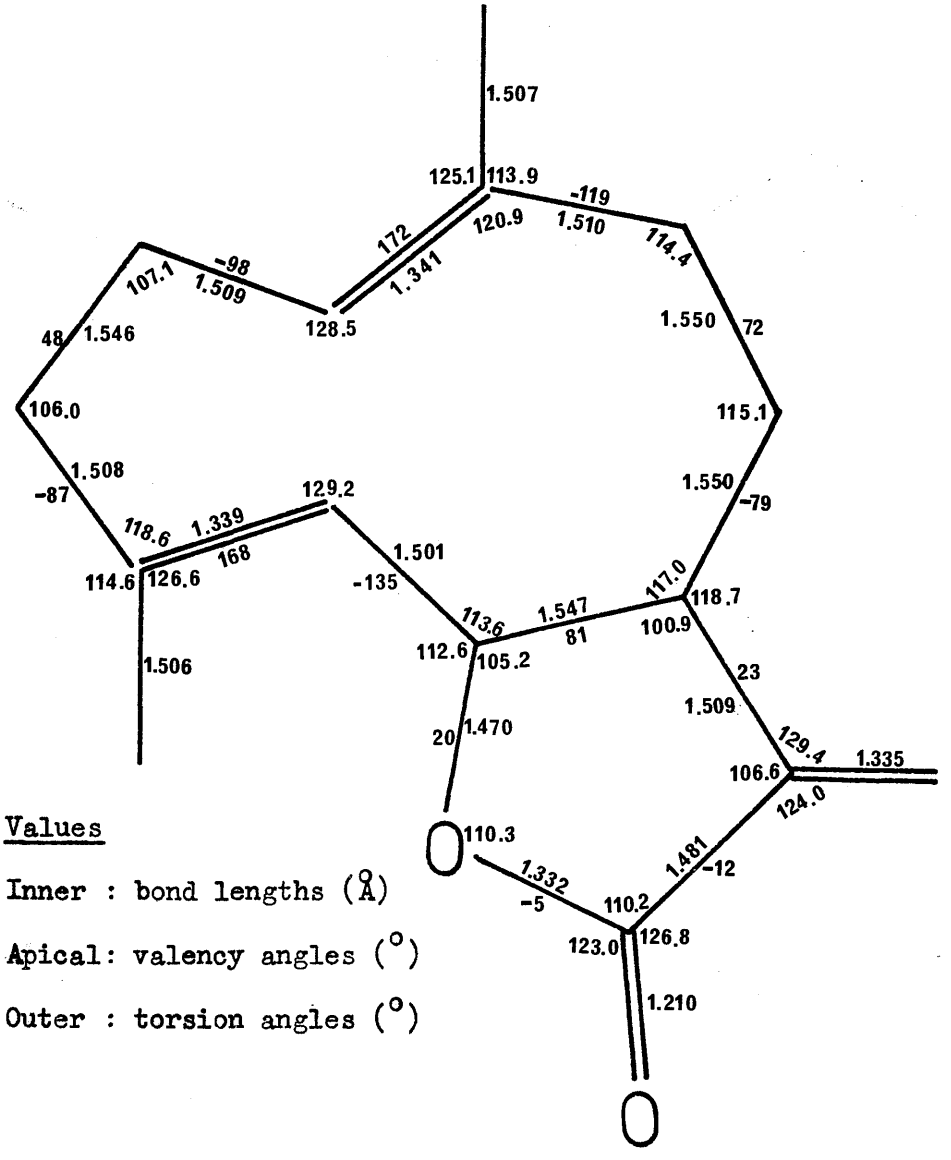
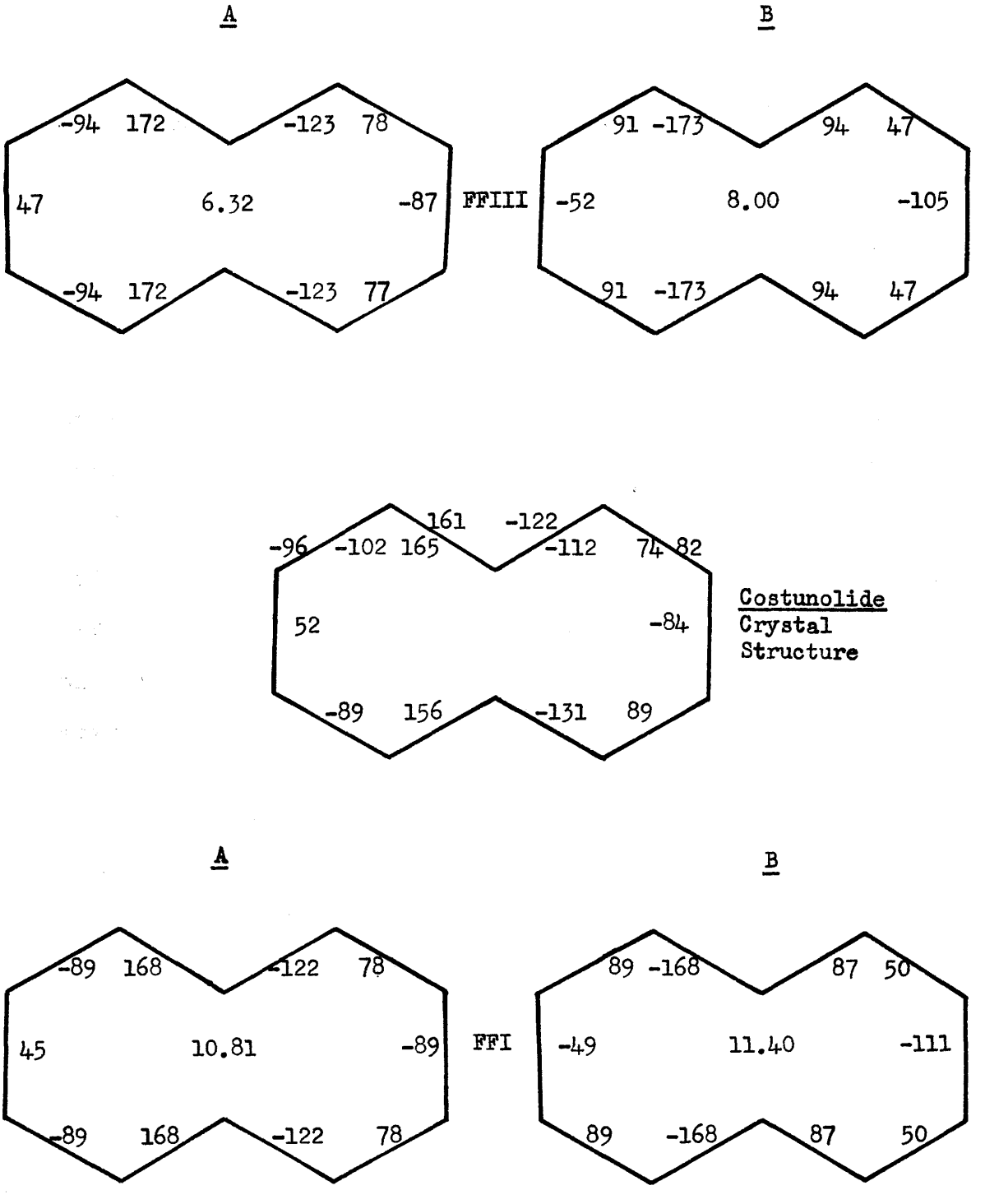


Fig. 6.4 Costunolide: Calculated Structure



Internal values: Peripheral - torsion angles(degrees)
Central - steric energies(K.cal/mole)
External values: torsion angles averaged to give C_2 symmetry.

Fig. 6.5 Energies and Conformations of A and B type Cyclodeca-1,5-diene

It is encouraging that both FFs give essentially the same stereochemistry and relative stabilities for the A and B conformation of I. This is not entirely unexpected since the main defect of Allingers parameterisation (FF III - alkane/alkene terms), namely overestimation of H ... H non-bonded interactions (28), is not important in these calculations. The conformation adopted by IX in the crystal (Fig. 6.2) is shown to be A and this conformation is about 1.5 K cal $mole^{-1}$ more stable than B (as typified by shiromodiol). Calculations have also been carried out for a number of other conformations of I using FFI none of which has proved more stable than A or B (27). The unsymmetrical substitution on the cyclodecadiene ring in IX forces a departure from the C_2 symmetry found in the calculation of I. If, however, the measured torsion angles are averaged so as to give a symmetric C_2 conformation of the macrocycle then the calculated and observed A structures lie within the limits of experimental error.

The results of these calculations thus provide a reasonable reference geometry for the two most stable conformations of I and they imply that the unequal deformations about the endocyclic C — C = C — C bonds observed in a number of germacranolides is caused by the substituents to I. In order to test this proposal additional strain energy calculations were performed for IX and X with FF III. The results are shown in Table II and it can be seen that while the torsional deformations have not been fully reproduced by calculation some support is given to the suggestion (4) that the more severe overcrowding

TABLE II CALCULATED AND OBSERVED GEOMETRIES IN THE VICINITY OF THE DOUBLE BONDS OF A AND B CONFORMATION CYCLODECADIENES.

COMPOUND		TORSION ANGLES *		NON-BONDED SEPARATIONS **			
		A1	A2	D1	D2	D3	D4
I	CONF. A	172	172	2.63	2.87	2.87	2.92
X	CONF. A	171	172	2.68	2.78	3.02	2.90
IX	CALC.	172	168	2.68	2.76	3.05	2.92
IX	X-RAY	164	156	2.83	2.96	3.26	3.20
I	CONF. B	173	173	2.72	2.92	2.92	2.89
X	CONF. B	172	172	2.64	2.85	3.15	3.26
XI	CALC.	172	173	2.64	2.86	3.15	3.26
XI	X-RAY +	163	153	2.88	3.03	3.00	3.11

CALCULATIONS PERFORMED WITH FFIII

* TORSION ANGLES IN DEGREES
A1 = C(2) - C(1) - C(10) - C(9)
A2 = C(3) - C(4) - C(5) - C(6)

** NON-BONDED SEPARATIONS IN ANGSTROMS
D1 = C(1)...C(4)
D2 = C(1)...C(5)
D3 = C(4)...C(10)
D4 = C(5)...C(10)

\+ THIS IS FOR DIHYDROMIKANOLIDE(7)

about C(4) - C(5) is responsible for the observed consistently greater twisting around this bond in germacranolides with skeleton A. Thus the calculated transannular distances for X represent those in the crystal structure much more closely than the corresponding separations in conformation A of I. The substitution of the trans-fused lactone at C(6), C(7) in IX does not significantly change these non-bonded distances. Calculations have also been carried out for XI and the corresponding conformation of X and a similar trend has been observed.

Therefore it seems probable that it is the substitution of the methyl functions at C(4) and C(10) that cause the observed torsional deformations about the Csp^2-Csp^2 bonds in the cyclodecadiene of conformation A. The failure of the FF to reproduce this particular geometrical aspect is disappointing but the exact form of the transannular interaction is so uncertain (4) that is is difficult to devise an FF which will accurately represent the balance of forces in this region. If the difference in the olefinic torsion angles is due to the substitution at C(4) and C(10) then x-ray analysis of derivatives of I (Conformation A) having bulky groups at these locations should also exhibit this deformation. No such analyses have been found in the literature but in 2,7-dibromo-3,8-dimethoxy-trans, trans-cyclodeca-1,6-diene (29) the bromine atoms are displaced outwards from the decadiene ring in a manner not unrelated to that of the methyl functions in IX.

6.4 Preferred fusion and conformation of the lactone ring

The observation of Yoshioka et al (13) regarding the preferred lactonisation of certain sesquiterpene lactones has been investigated by MM. Calculations were carried out for the A and B conformation of compounds IX - XIII and the results (Table III) confirm that the C(7) - C(8) —— trans-fused lactone with an oxygen function at C(6) is more stable than the corresponding C(6) - C(7) —— fused isomer with an oxygen function at C(8).

The explanation for this behaviour can be found on examination of the steric environment of the lactone ring at each site. Cleavage of the O - CO bond of the δ— lactone of XII or XIII reduces the strain on the cyclodecadiene ring which will relax to a conformation much closer to A or B. It does not appear to be possible for the macrocycle to change from B to the more stable A under these circumstances because the substituents impose severe steric restrictions on such a conformational change.

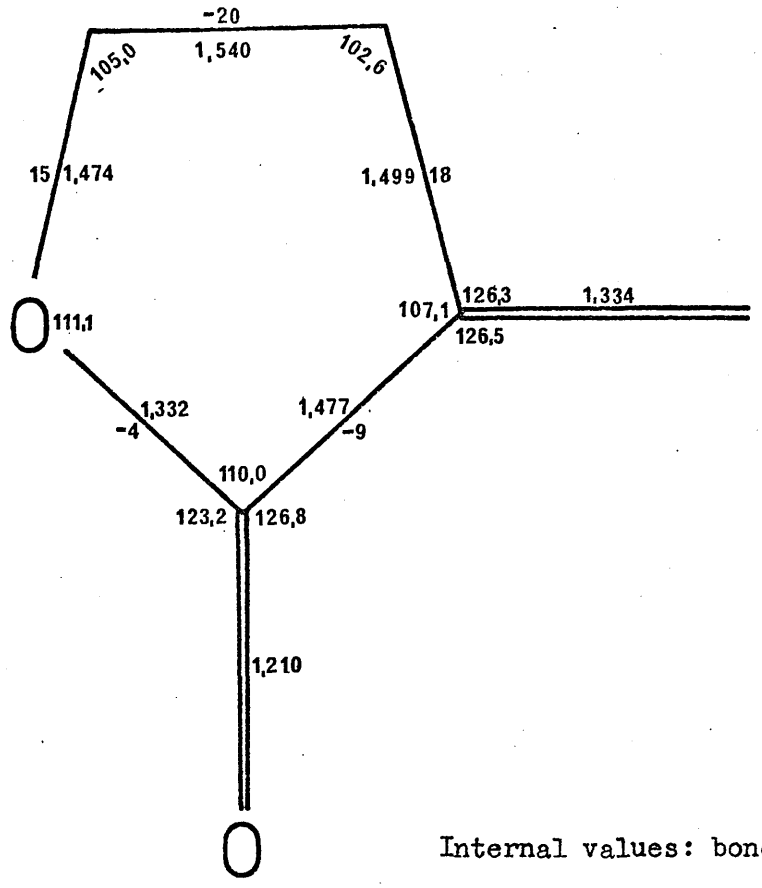
The major factor influencing the choice of sites now available for relactonisation is the amount of strain arising from the constraints imposed by trans-fusion of the alkene and lactone rings. The minimum energy conformation of an isolated δ - lactone (XIV) was obtained by strain energy calculations (Fig. 6.6). The endocyclic torsion angle about the Csp^3 - Csp^3 bond of XIV is 20^o in its most stable conformation and therefore fusion to the cyclodecadiene ring should be accommodated most easily when the appropriate torsion angle of the ten-membered ring is also about 20^o.

TABLE III STERIC ENERGIES OF SOME GERMACRANOLIDE LACIONES

COMPOUND	C(13) METHYLENE A	C(13) METHYLENE B	C(13) METHYL + A	C(13) METHYL + B	C(13) METHYL ++ A	C(13) METHYL ++ B
			ENERGIES			
IX	15.9	20.4	---	---	11.2	---
X	9.1	10.9	9.1	10.9	9.1	10.9
XI	14.6	14.5	9.5	---	---	---
XII	18.7	21.8	12.6	16.1	12.9	19.1
XIII	16.9	16.2	11.5	13.6	11.4	14.6
			ENERGY DIFFERENCES			
XII - XIII	1.8	5.6	1.2 *	1.5 *	1.4 **	5.5 **
IX - XI	1.3	5.9	---	---	1.7 **	---

ALL ENERGIES IN K.CAL/MOLE

+	ALPHA METHYL	
++	BETA METHYL	
*	C(13) ALPHA TO BETA	SEE TEXT
**	C(13) BETA TO ALPHA	SEE TEXT



Internal values: bond lengths(Å)

Apical values: valence angles(°)

External values: torsion angles(°)

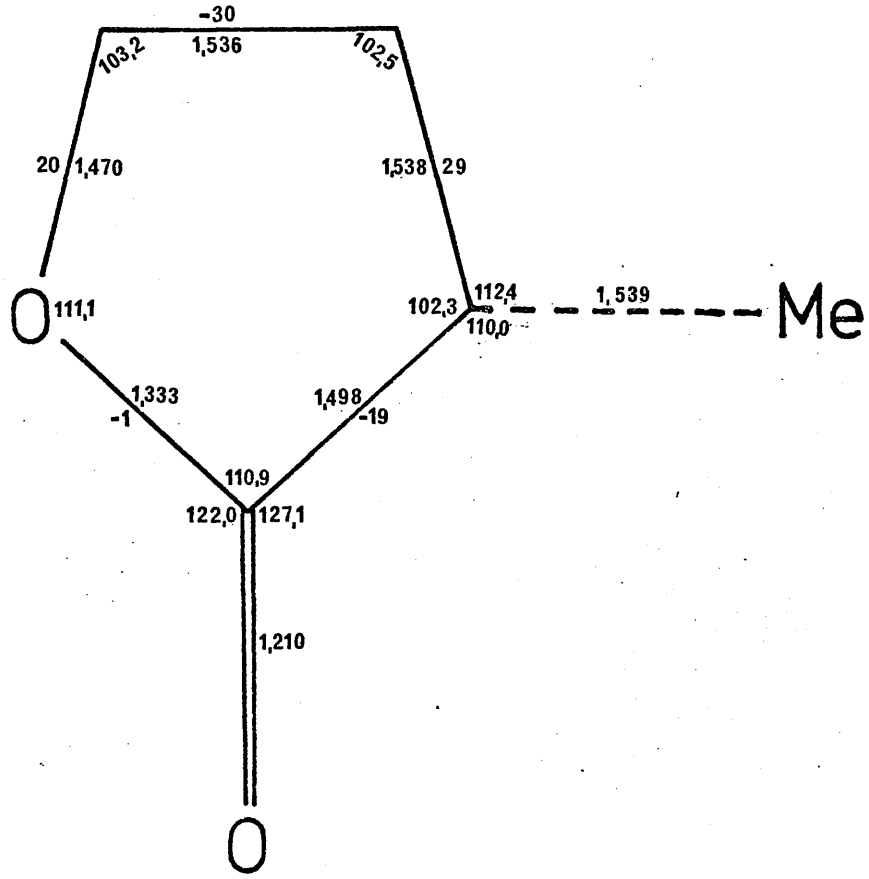


Fig. 6.6 Calculated minimum energy geometries for XIV and one of its C(13)- methyl analogues

Newman projections down (i) the C(6) - C(7) and (ii) the C(7) - C(8) bonds of the calculated structures for the A and B conformations of 1,5-dimethyl-cyclodeca-1,5-diene (X) are illustrated in Fig. 6.7. The locations for subsequent lactone fusion are shown by broken lines. For the B conformations it is quite clear that C(7) - C(8) fusion is to be preferred since the relevant torsion angles are -59° and -3°at (i) and (ii) respectively. Compound XIII therefore represents the minimum energy structure for the B conformation and it is interesting to note that the additional strain is accomodated mainly by the lactone ring deforming so that it is almost planar (Fig. 6.8). However, the planar lactone ring is not as unstable as might be anticipated since the endocyclic valence angles move closer to 108° and this is nearer to their unstrained values ($109 - 120^{\circ}$) than in XIV thus reducing the Baeyer strain. Also the minimum Pitzer strain is at 0° for all the bonds of the lactone except the single Csp^3- Csp^3 bond where it is maximised. Although the planar lactone is less favourable than the puckered conformation in isolation it appears that in a gross structure such as the B conformation of XIII it can represent the minimum energy stereochemistry. It has been observed experimentally in the x-ray analyses of elephantol (5) and a derivative of florilenalin (31).

C(7) - C(8) trans-fusion of the α-methylene -γ- lactone is also preferred for the A conformation. The difference between the appropriate torsion angles ((1) -44°, (11) 38°) is not enough to account for the 1.8 K.cal per mole energy differential between the A conformations

Fig. 6.7

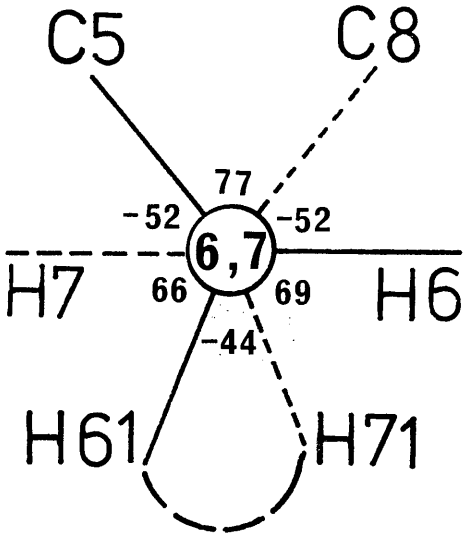
Newman projections down the C(6)-C(7) and C(7)-C(8) bonds for the calculated structures of the A and B type conformations of dimethylcyclodeca-1,5-diene.

(a) C(6)-C(7) A type

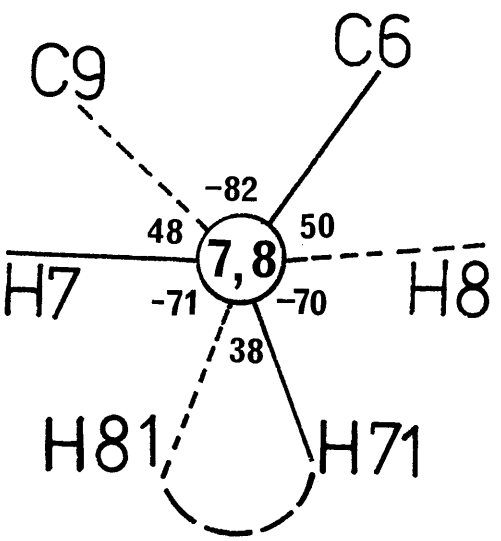
(b) C(7)-C(8) A type

(c) C(6)-C(7) B type

(d) C(7)-C(8) B type

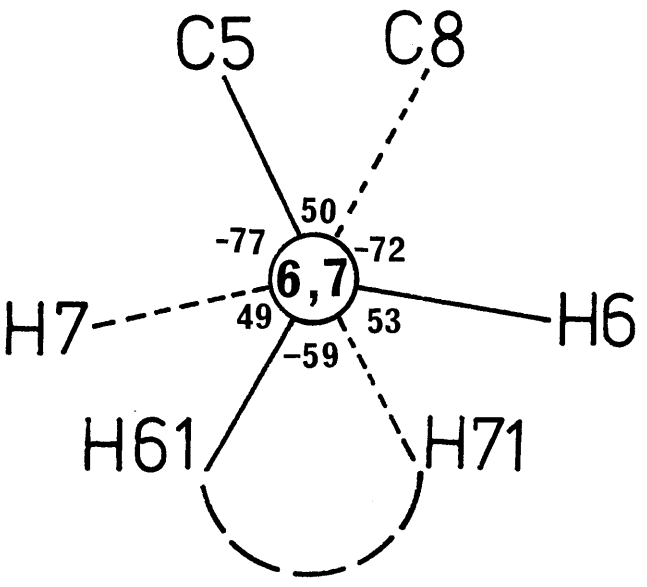

C5
C8
77
-52
-52
6,7
H7
66
69
H6
-44
H61
H71

(a)


C9
C6
-82
48
50
7,8
H7
-71
-70
H8
38
H81
H71

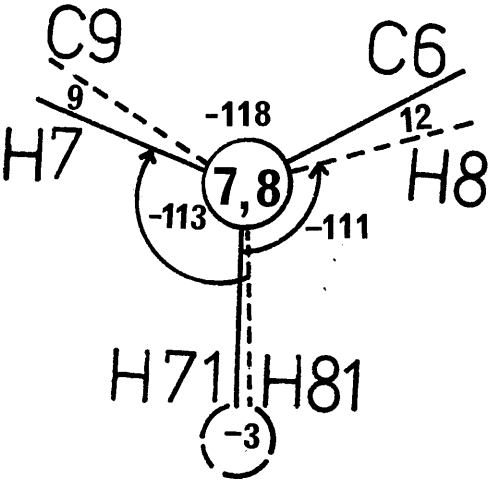
(b)

A


C5
C8
50
-77
-72
6,7
H7
49
53
H6
-59
H61
H71

(c)

B


C9
C6
9
-118
12
H7
7,8
H8
-113
-111
H71
H81
-3

(d)

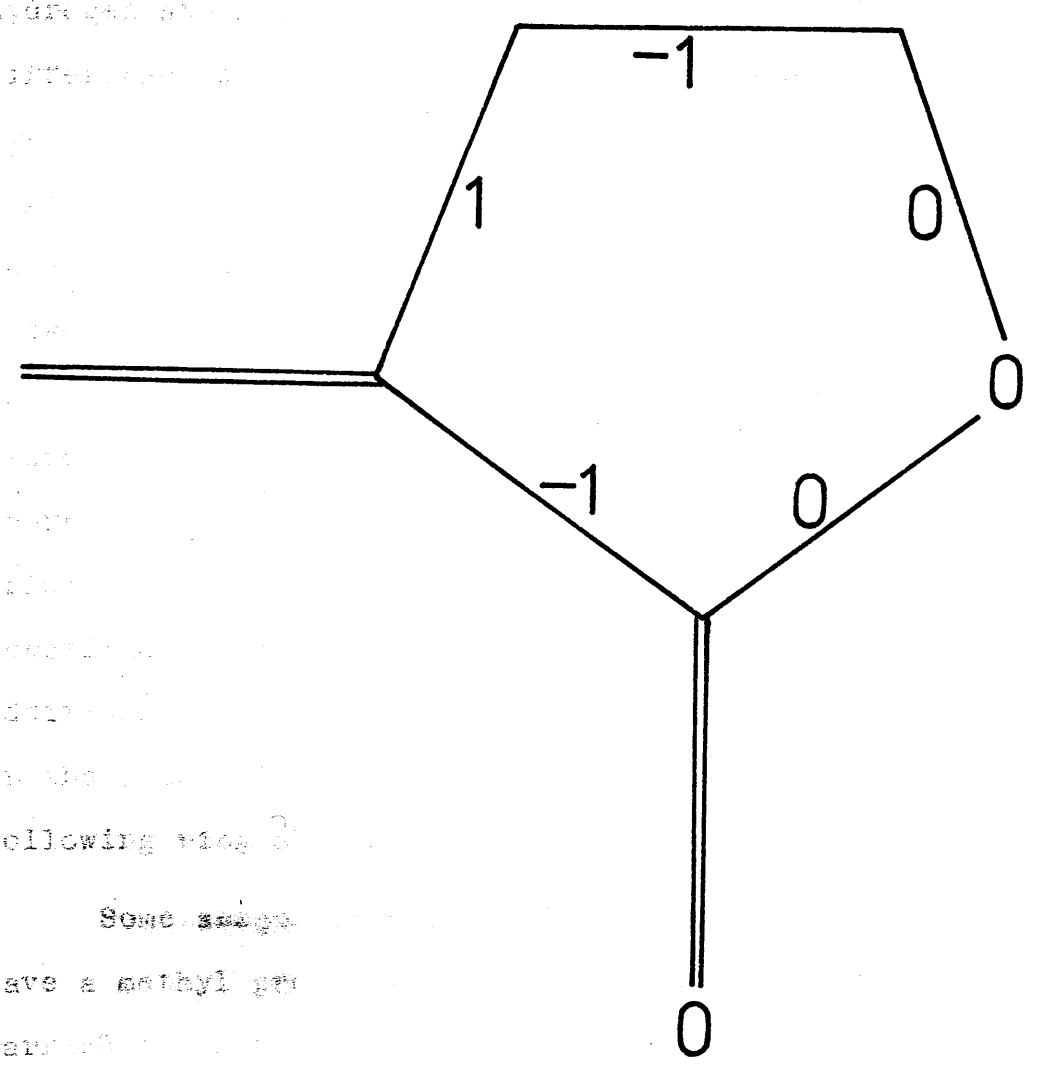


Fig. 6.8 Calculated torsion angles(°) for lactone in XIII (B)

of XII and XIII (Table III). Further investigation has indicated that there is a secondary stabilising effect for the C(7) - C(8) fusion arising from the distinct steric environments of the hydroxyl group at C(6) and C(8). If the hydroxyl functions in XII and XIII are replaced by hydrogen atoms (IX and XI) then the relevant energy difference is 1.4 k cal per mole. Complete removal of the $\underline{\alpha}$- hydrogen at C(6) or C(8) in these latter two compounds further reduces this difference to 0.4 k cal per mole. This suggests that the C(6) $\underline{\alpha}$-hydroxyl is in a less crowded environment than the $\underline{\alpha}$- hydroxyl at C(8). The main reason for this is the interaction between the C(8) hydroxyl and the hydrogens attached to C(9) (Table IV). There is only one hydrogen at the sp^2 C(5) so that this effect is considerably reduced for the C(6) hydroxyl substituent and consequently relactonisation at C(8) is additionally stabilised. There is a much smaller difference in the alternative environments of the ester oxygen atom following ring closure.

Some sesquiterpene lactones (e.g. dihydromikanolide) have a methyl group at C(11) and calculations have been carried out for the corresponding $\underline{\alpha}$-methyl isolated lactone (Fig. 6.6) and for the $\underline{A}$ and $\underline{b}$ conformations of IX - XIII with $\underline{\alpha}$- and $\underline{\beta}$-methyl substitution at C(11) to confirm the generality of the preferred C(8) relactonisation. When the methylene group at C(11) is replaced by a methyl function, rotation about the C(11) - C(13) bond can relieve strain and thus reduce the H(C13) ... O(hydroxyl) interaction (Table IV). Also C(11) is now sp^3 changing the

TABLE IV CONFORMATION A: SOME NON-BONDED INTERACTIONS INVOLVING THE HYDROXYL FUNCTION

FUSION C(6) - C(7)		FUSION C(7) - C(8)	
ATOMS	SEPARATION *	ATOMS	SEPARATION *
C(9)...H(O16)	2.53	C(5)...H(O17)	2.47
O(16)...H(C7)	2.69	O(17)...H(C7)	2.74
O(16)...H(C9)	2.63	O(17)...H(C5)	2.75
O(16)...H'(C9)	2.63	---	---
O(16)...H(C13)	2.30	O(17)...H(C13)	2.32
H(C8)...H(O16)	2.20	H(C6)...H(O17)	2.23
H'(C9)...H(O16)	2.34	H(C5)...H(O17)	2.75

* IN ANGSTROMS

O(16) - H(O16) IS THE HYDROXYL GROUP AT C(8) IN C(6) - C(7) FUSED LACTONES
O(17) - H(O17) IS THE HYDROXYL GROUP AT C(6) IN C(7) - C(8) FUSED LACTONES

INTERACTIONS READING ACROSS THE PAGE ARE EQUIVALENT.
THUS C(9)...H(O16) IS EQUIVALENT TO C(5)...H(O17) FOR C(7) - C(8) FUSION

minimum of several torsional interactions from 0° to 60°. The net result is that the isolated α-methyl lactone is more stable (than the methylene) by 3.0 K.cal per mole. The calculated energies for the gross structures (Table III) show that C(7) - C(8) fusion is once again more favourable, although the relevant energy differences are generally smaller. Comparison of isomers is a little more complicated because, for instance, a C(6) - C(7) fused compound with C(13) α-methyl would, on relactonisation to C(7) - C(8) fusion have the C(13) methyl β (Fig. 6.9). The energy differences quoted in Table III allow for this additional constraint.

The experimental work of Yoshioka et al is therefore supported by these strain energy calculations which extend the range of compounds to which the relactonisation rule can be applied.

The preceding discussion on lactone fusions in germacranolides does not consider the possibility of cis-fusion. If it is assumed as in all known germacranolides, that C(7) - C(11) is always β then H(6) and H(8) (Fig. 6.7) represent the alternative locations at which lactonisation could occur. For conformation A of X the appropriate torsion angles of 69° and -70°, for C(6) and C(8) fusion respectively, are very much further away from the minimum conformation of the isolated lactone than the torsion angles which would be involved in trans- fusion. This is reflected in the higher strain energy of 20.6 K.cal per mole for the cis-lactone isomer of XII compared

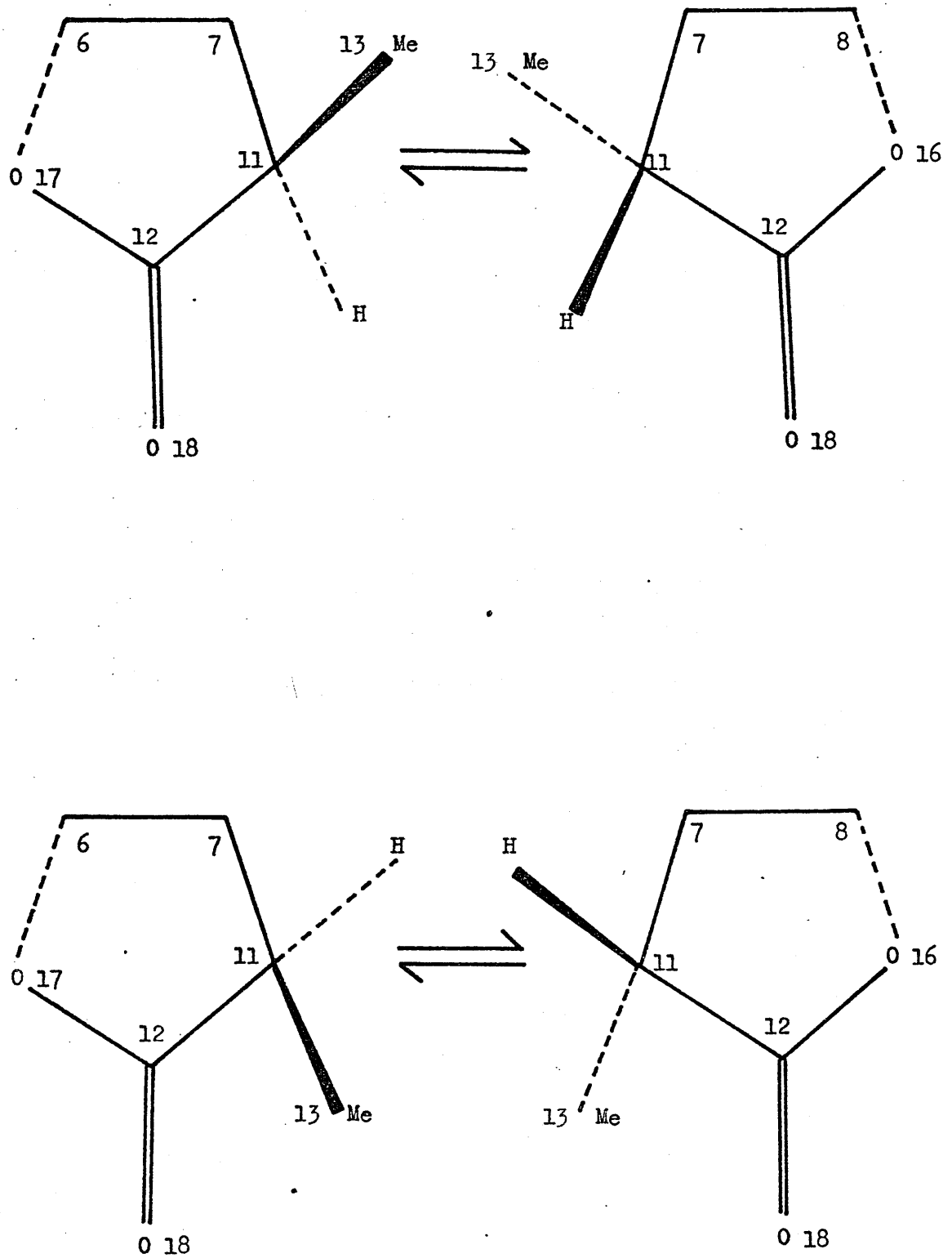


Fig. 6.9 Relationships between stereochemistry at C(11) and lactone fusion

with the corresponding value of 18.7 K.cal per mole for the trans-fused lactone.

In the B conformation of X cis-fusion at C(8) is extremely unfavourable (Fig. 6.7) and the much smaller value of the relevant torsion angle at C(6) (59^{o}as opposed to -111^{o}) makes this latter site the most acceptable.

The proposals made in this section regarding the energetically favoured sites for lactone fusion are based on the assumption that the lactone ring retains a geometry close to that of the calculated energy minimum. This supposition was tested by applying the algorithm of Cremer and Pople (32) to a number of calculated and observed structures. The results in terms of their parameter $\emptyset$ are listed in Table V, and show that there is a remarkable consistency in the conformation of the lactone ring in a range of very different germacranolides. This conformation appears, for the examples quoted, to be independent of:

(i) The mode of fusion. Unfortunately the very unfavourable 7,8 cis fusion is not represented but the 6,7 cis- and the trans- fused lactones show little variation in conformation.

(ii) The group substituted at C(11) even when there is a very bulky group at C(8) e.g. in Eupatoriopicrin (34).

(iii) The conformation of the macrocycle of the germacranolide.

The values listed in Table V also indicate the location of the conformation on the pseudorotational

TABLE V CONFORMATION OF THE LACTONE RING IN SOME GERMACRANOLIDES

COMPOUND	TYPE *	C(13) **	ALPHA ***	PHI ##	A$ PSI	GAM	PHI ##	B$ PSI	GAM
CALCULATIONS									
ISOLATED LACTONE $$	---	M1	---	10	-9	-20	---	---	---
ISOLATED LACTONE $$	---	M2	---	1	---	-30	---	---	---
IX	6,7T	M1	H	10	-11	-26	11	-12	-29
---	6,7T	M3	H	1	---	---	---	---	---
XII	6,7T	M1	OH	8	-15	-29	13	-9	-26
---	6,7T	M2	OH	2	---	-30	-1	---	---
---	6,7T	M3	OH	-3	---	-33	1	---	---
XI	7,8T	M1	H	10#	10	23	PL	0	0
---	7,8T	M2	H	1#	---	---	---	---	---
XIII	7,8T	M1	OH	9#	13	27	PL	-1	-1
---	7,8T	M2	OH	-1#	---	32	-14#	---	12
---	7,8T	M3	OH	0#	---	32	-9	---	-16
---	6,7C	M1	OH	9#	16	34	---	---	---
CRYSTAL STRUCTURES									
COSTUNOLIDE(4)	6,7T	M1	H	17	-10	-25	---	---	---
ALATOLIDE(6)	6,7T	M1	OXY	23	0	-19	---	---	---
EUPATOLIDE(34)	6,7T	M1	OXY	15	-12	-27	---	---	---
EUPATORIOPICRIN(35)	6,7T	M1	OXY	5	-9	-24	---	---	---
ONOPODOPICRINE(35)	6,7T	M1	OXY	11	1	-16	---	---	---
DIHYDROMIKANOLIDE(7)	7,8T	M2	OXY	---	---	---	1#	---	31
ELEPHANTOL(5)	7,8T	M1	OXY	---	---	---	PL	11	33

SYMBOLS EXPLAINED ON FOLLOWING PAGE

EXPLANATION OF SYMBOLS IN TABLE V

*	OF FUSION OF LACTONE TO CYCLODECADIENE E.G. 6,7T MEANS C(6) - C(7) TRANS-FUSED E.G. 7,8C MEANS C(7) - C(8 CIS-FUSED
**	SUBSTITUTION AT C(11) M1 C(13) IS =CH2 M2 C(13) IS ALPHA METHYL M3 C(13) IS BETA METHYL
***	SUBSTITUTION AT THE ALPHA POSITION OF C(6)/C(8) FOR 6,7/7,8 FUSION
$	'PHI' (DEGREES) CALCULATED WITH ALGORITHM OF CREMER AND POPLE(32) BASE VALUE (0) IS THE ALPHA-C(7) ENVELOPE INTERVAL BETWEEN ENVELOPES/HALF CHAIRS IS 18 DEGREES 'GAM' (DEGREES) IS THE ENDOCYCLIC C-C-C-O TORSION ANGLE OF THE LACTONE RING 'PSI' (DEGREES) IS THE EXOCYCLIC C=C-C=O TORSION ANGLE OF THE LACTONE RING
$$	RESULTS FOR ISOLATED LACTONES GIVEN UNDER A CONFORMATION FOR CONVENIENCE
#	PHI IS EQUAL TO OR GREATER THAN 180 DEGREES THEREFORE ROTATION IS FROM BETA-C(7) ENVELOPE
##	SIGN OF PHI GIVES ROTATION FROM C(7) ENVELOPE + IS ANTICLOCKWISE 6,7 FUSION - IS CLOCKWISE 6,7 FUSION + IS CLOCKWISE 7,8 FUSION - IS ANTICLOCKWISE 7,8 FUSION
PL	PLANAR LACTONE RING
OXY	NON-HYDROXYL OXYGEN FUNCTION E.G. ESTER

circuit. Thus in an isolated 5-membered cycle it is possible to have the puckering (e.g. for an envelope) $\underline{\alpha}$ or $\underline{\beta}$- orientated so that a calculated geometry for an isolated cyclopentane is not unique because there is an isoenergetic isomer in which all the torsion angles have their signs reversed. In the isolated $\underline{\gamma}$-lactone with methylene substitution at C(11) (Fig. 6.6) the mirror image is also isoenergetic and the five-membered ring can adopt $\underline{\alpha}$ or $\underline{\beta}$ puckering with equal ease. When the C(11) substitution is methyl (M2 or M3 in Table V) there will be a small difference in stability between the mirror-image related conformations. The results in Table V show that the lactone conformation in germacranolides generally approximates to a C(7) envelope (in this context this includes the half-chairs in which C(7) is one of the out of plane atoms). The major exception to this being the occurrence of planar stereochemistry when the conformation of the macrocycle makes this more stable.

Further, 6,7 trans-fused germacranolides should adopt a C(7) $\underline{\alpha}$-puckered envelope conformation of the five-membered ring independant of the conformation (A or B) of the macrocycle while the 7,8 trans-fused isomer (A conformation) should be $\underline{\beta}$. The A conformation crystal structures listed in Table V all obey this rule.

The values of the lactone ring torsion angles $\underline{\Psi}$ (C═C—C═O) and $\underline{\Phi}$ (endocyclic C—C—C—O) are also shown in this table and the reported correlation (33) between these two angles is observed in all the compounds investigated. $\underline{\Psi}$ and $\underline{\Phi}$ are also related to the Cremer and Pople angle $\underline{\phi}$ and the sign of $\underline{\Phi}$ (+ or -) can be used as a

predictor of the lactone puckering ($\underline{\beta}$ or $\underline{\alpha}$ respectively). Examination of Dreiding models indicates that, for lactone conformations close to a C(7) envelope, this latter correlation is exactly what would be expected.

The reasons for the relationship between the lactone puckering and the mode of fusion (6,7 trans or 7,8 trans) with the dimethyl cyclodecadiene can be elucidated from Fig. 6.7. The minimum energy conformation of the isolated lactone XIV (Fig. 6.6) has $\Phi = -20$ and the existence of an isoenergetic isomer with $\Phi = +20$ has been noted above. The stereochemistry about the C(6) - C(7) bonds of both A and B conformations of X is very similar and in particular the H(61)—C(6)—C(7)—H(71) torsion angles are negative (-44° and -59° respectively) and hence 6,7 trans lactonisation is facilitated with the $\Phi = -20$ enantiomer resulting in $\underline{\alpha}$ puckering. The relevant torsion angle for 7, 8 trans-lactonisation for conformation A is 38° resulting in $\underline{\beta}$ puckering. The corresponding torsion angle in the B conformation is -3° and the lactone ring is able to adopt $\underline{\alpha}$, $\underline{\beta}$, or planar stereochemistry. (Table V). On this basis prediction can also be made for the cis-fused lactones, which have so far not been observed in nature, by considering the H(6)—C(6)—C(7)—H(71) torsion angles of X. For instance a 6,7 cis fused germacranolide with an A conformation of X should be $\underline{\beta}$ puckered. The calculated minimum energy conformation of such a structure has a $\underline{\beta}$ puckered lactone ring (Table V). It should also be possible to extend this approach to account for lactone conformations in other sesquiterpenes once the ground state of the main carbon skeleton has been

TABLE VI SUMMARY OF RESULTS IN SEC. 6.4

PREFERRED FUSION OF LACTONE	CONFORMATION A 7,8 TRANS	CONFORMATION B 7,8 TRANS
LACTONE STEREOCHEMISTRY		
ENDOCYCLIC C-C-C-O TORSION ANGLE	+	BETA PUCKER
ENDOCYCLIC C-C-C-O TORSION ANGLE	-	ALPHA PUCKER

CORRELATION BETWEEN LACTONE STEREOCHEMISTRY,
MODE OF FUSION, AND CYCLODECADIENE CONFORMATION

	CONFORMATION A	CONFORMATION B
6,7 TRANS	ALPHA	ALPHA
6,7 CIS	BETA	BETA
7,8 TRANS	BETA	*
7,8 CIS	ALPHA	ALPHA

THESE RESULTS ASSUME THAT THE LACTONE CONFORMATION IS CLOSE TO THE MINIMUM ENERGY STEREOCHEMISTRY OF THE ISOLATED LACTONE AND THAT THE C(7) - C(11) BOND IS ALWAYS BETA

* CAN BE ALPHA, BETA, OR PLANAR . SEE TEXT.

obtained. The substitution at C(11) (methyl or methylene) appears to make very little difference to the puckering of the lactone ring except when the relevant torsion angle on the larger carbocycle is close to 0^{o}(as for 7,8 fusion of B conformation germacranolides.)

The conclusions made in this section are summarised in Table VI.

6.5 The C═C—C═O chromophore

The relationship between the stereochemistry of lactone ring fusion and the sign of the Cotton effect at 250 - 260 nm, and also its apparent correlation with the endocyclic C — C — C — O (Φ) and exocyclic C═C — C═O (Ψ) torsion angles has been noted previously (e.g. 4, 6, 15, 36). Cox and Sim (6, 33) have questioned the relevance of the Beecham correlation (15) between the sign of the Cotton effect and the chirality of the C═C—C═O chromophore as a result of the observed value (Ψ = 0) obtained for alatolide. The recent determination of the structure of onopordopicrine found a Ψ of 1^{o} with an estimated error of 0.5^{o} (34) giving rise to further doubts since Beecham predicted that such compounds should have left handed chirality of the C═C—C═O group (Ψ negative). Further, the results in the previous section support the view of Cox and Sim, since a direct correspondence has been shown between Φ and the mode of lactone fusion for A and B type germacranolides. Thus there is a relationship between the sign of Φ (as assigned by Cox and Sim (6), McPhail and Sim (33)), the

correlation of Stöcklin et al (15) between the sign of the Cotton effect and the stereochemistry and location of lactone fusion, and the prediction of Section 6.4 (Table VII).

The value of $\underline{\Psi}$ appears to be less important than $\underline{\Phi}$ and the wide range in the magnitude of $\underline{\Psi}$ suggests a degree of flexibility about the C(11) - C(12) bond.

In the isolated molecule XIV the minimum stereochemistry is a C(7) envelope (Fig. 6.6) and the isoenergetic $\underline{\alpha}$-and $\underline{\beta}$-envelopes are observed (from Dreiding models) to have $\underline{\Phi}$ and $\underline{\Psi}$ paired in sign . The calculation of the $\underline{\alpha}$-envelope, for instance, gives values of - 20 and - 9° respectively. Thus to a first approximation the chiralities are interdependant. The minimum energy XIV still has some bad van der Waals repulsions (C(13)... H(7^1), 2.82A°; H(7)...H(6^1), 2.43A°; and C(13)...O(18), 3.00A°) which may become more severe in a sesquiterpene. The angle $\underline{\Psi}$ has the minimum torsional interaction at 0° and the value of -9° in the isolated lactone is caused by an attempt to minimize the two bad C(13) non-bonded interactions (H(7^1) and O(18) are directed towards opposite faces of the lactone). Clearly the variation of steric energy with $\underline{\Psi}$ in a sesquiterpene is dependant on the degree to which these (and other) interactions can be minimized in a specific environment and this should be reflected in the range of observed $\underline{\Psi}$.

The method of Wiberg and Boyd (37) has been used to pseudorotate $\underline{\Psi}$ at 3° intervals for the $\underline{A}$ and $\underline{B}$ conformations of XII and XIII and the results are plotted in Fig. 6.10. With the exception of the minima, the calculations were

TABLE VII RELATIONSHIPS BETWEEN THE LACTONE STEREOCHEMISTRY AND THE COTTON EFFECT AT 260N NM.

LACTONE FUSION	SIGN OF CE *	SIGN OF GAMMA CS & MS +	SIGN OF GAMMA G $
6,7 TRANS	-	-	-
7,8 TRANS	+	+	+
6,7 CIS	+		+
7,8 CIS	-		-

GAMMA IS THE ENDOCYCLIC C-C-C-O TORSION ANGLE

* CORRELATION OF STOCKLIN ET AL(14)

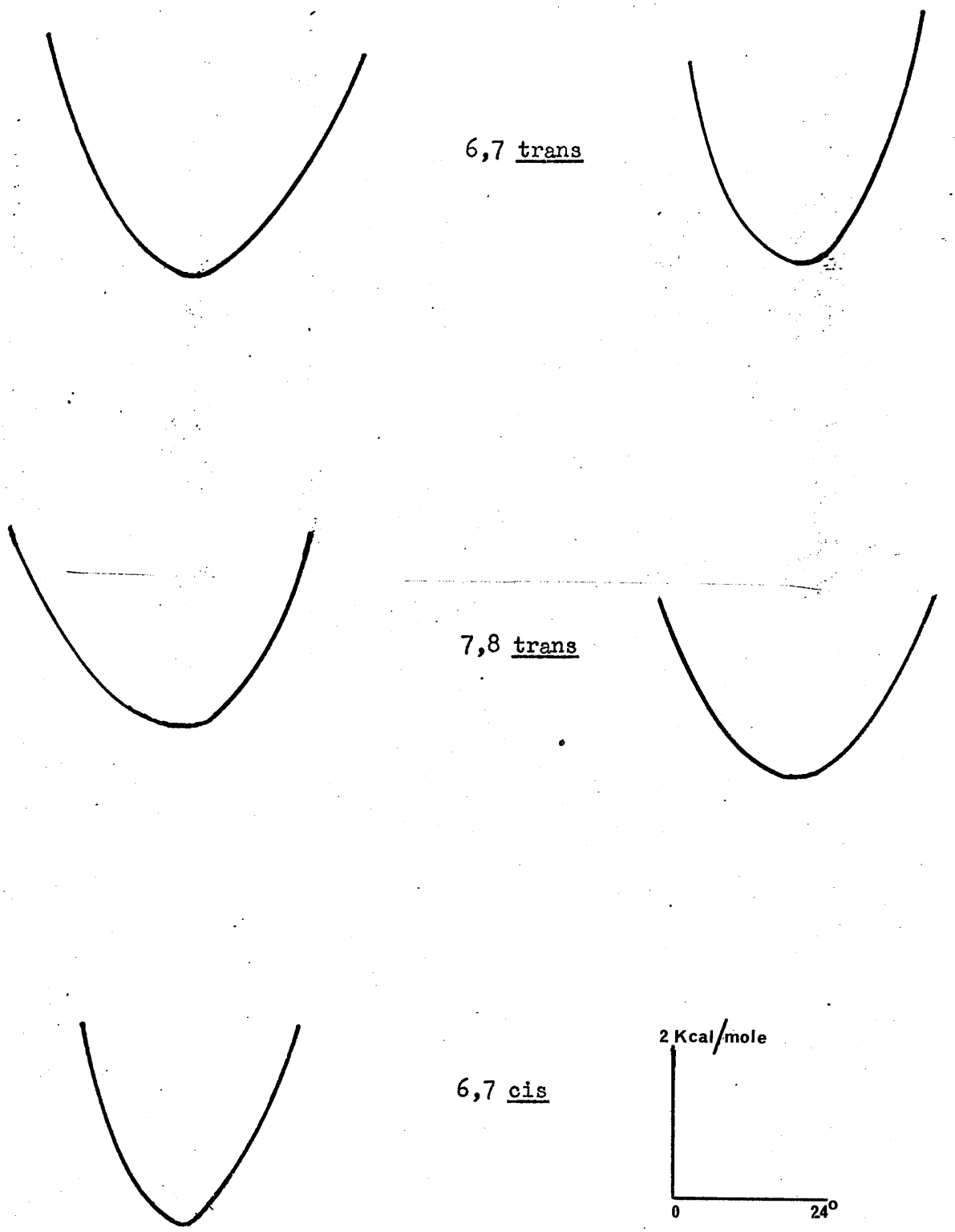
\+ AS ASSIGNED BY COX AND SIM(6),MCPHAIL AND SIM(33)

$ AS REPORTED IN THIS THESIS.APPLICABLE ONLY TO THE A AND B CONFORMATIONS OF GERMACRANOLIDES

Conformation A

Lactone Fusion

Conformation B



Ordinate: Energy

Abcissa : Exocyclic C=C-C=O torsion angle (psi)

Fig. 6.10 Variation in energy with psi for various germacranolides

performed to block diagonal convergence only (17). In germacranolides with the A conformation $|\underline{\psi}|$ varies by about 15° (Table V) and the calculated increase in steric energy at $\pm 15^{\circ}$ from the minimum in each of the calculated structures is given in Table VIII. This table also includes the results for a 6,7 cis fused A type germacranolide.

There is a correspondence between the flexibility in $\underline{\psi}$ and the ease or otherwise of lactonisation of the appropriate dimethyl cyclodecadiene (Section 6.4). The strain present in a 6,7 trans fused B conformation— and 6,7 cis fused A conformation— is clearly reflected in the additional strain induced when $\underline{\psi}$ is removed from its value in the minimum energy structure (as shown by the steeper-sided potential wells for these structures in Fig. 6.10). In the other compounds a certain amount of flexibility is apparent and it is also evident that for the A conformations, in particular, variation of $\underline{\psi}$ in one direction (positive or negative) is more favourable than in the other. Thus it would be expected that for 6,7 trans fused A type germacranolides most compounds would have $\underline{\psi}$ within the range 0 to -15° ($\underline{\psi}^{+} = 0.4$, $\underline{\psi}_{min} = -15$).

The observed $\underline{\psi}$ in the corresponding structures in Table V ranges from -10 to +1. The energy difference between the minimum and one of the extrema is about 1 K.cal $mole^{-1}$ for most of the structures in Table VIII.

TABLE VIII VARIATION OF STERIC ENERGY WITH PSI

COMPOUND	PSI(MIN) A	PSI(MIN) B	RELATIVE ENERGIES $ A PSI+	RELATIVE ENERGIES $ A PSI-	RELATIVE ENERGIES $ B PSI+	RELATIVE ENERGIES $ B PSI-
VIII	-15	-9	0.4	1.5	>5.0 *	2.0
IX	13	-1	1.5	0.8	1.1	1.3
VIII(CIS)	16		2.0	3.2 *		

$ K.CAL/MOLE

CIS THIS IS THE CIS FUSED ISOMER OF VIII

* INTERPOLATED VALUE.STEEP GRADIENT TO CURVE AND CALCULATION DID NOT EXTEND TO 15 DEGREES FROM MINIMUM

PSI IS THE EXOCYCLIC C=C-C=O TORSION ANGLE (DEGREES)
PSI(MIN) IS THE VALUE OF PSI IN THE MINIMUM ENERGY STRUCTURE
PSI+ DIFFERENCE BETWEEN STRAIN ENERGY AT PSI(MIN) AND AT PSI(MIN + 15)
PSI- DIFFERENCE BETWEEN STRAIN ENERGY AT PSI(MIN) AND AT PSI(MIN - 15)

6.6 References

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APPENDIX A

FFI GLASGOW ALKANE/ALKENE FORCE FIELD

ATOM KEY

1 = H, 2 = C(SP)**2, 3 = C(SP)**3,

FORCE CONSTANTS ARE IN KCAL/MOLE/ANGSTROM**2 OR IN KCAL/MOLE/DEGREE**2
ENERGIES ARE IN KCAL/MOLE

BOND STRETCHING

EXPRESSION: EB=STRETCHK1*(LENGTH-REF.LENGTH)**2

TYPE1	TYPE2	STRETCHK1	REF.LENGTH
1	2	346.0000	1.0890
1	3	331.2000	1.1000
2	2	670.0000	1.3350
2	3	319.5000	1.5010
3	3	316.8000	1.5200

VAN DER WAALS

EXPRESSION: EV=((-2.0*EPSILON)/(ALPHA)**6)+(EPSILON*EXP(12.0*(1.0-ALPHA)))

ALPHA=DIST(1-2)/(RSTAR1+RSTAR2)

TYPE1	TYPE2	RSTAR1	RSTAR2	EPSILON
1	1	3.1000	0.0	0.0160
1	2	3.5300	0.0	0.0330
1	3	3.3500	0.0	0.0299
2	2	4.0000	0.0	0.0760
2	3	3.6000	0.0	0.0800
3	3	3.8500	0.0	0.1200

ANGLE BENDING

EXPRESSION: EA=BENDK1*(((DELTH)**2)-(BENDK2*(DELTH)**3))

DELTH=ABS(REF.ANGLE"N"-OBSERVED ANGLE)
REF.ANGLE"N" IS USED FOR DEGREE OF NON-HYDROGEN SUBSTITUTION "N" ON THE CENTRAL ATOM OF THE ANGLE CONCERNED.ANGLES ARE IN DEGREES

TYPE1	TYPE2	TYPE3	BENDK1	BENDK2	REF.ANG1	REF.ANG2	REF.ANG3	REF.ANG4
1	2	1	0.0055	0.0096	118.6000	0.0	0.0	0.0
1	2	2	0.0060	0.0	121.7000	120.4000	0.0	0.0
1	2	3	0.0060	0.0	0.0	117.5000	0.0	0.0
2	2	3	0.0120	0.0096	0.0	122.3000	121.0000	0.0
3	2	3	0.0233	0.0096	0.0	0.0	116.4000	0.0
1	3	1	0.0072	0.0096	108.2000	109.1000	0.0	0.0
1	3	2	0.0088	0.0096	110.5000	110.0000	110.2000	0.0
1	3	3	0.0088	0.0096	109.5000	109.0000	109.2000	0.0
2	3	2	0.0090	0.0096	0.0	111.0000	110.1000	109.5000
2	3	3	0.0090	0.0096	0.0	110.4000	110.1000	109.5000
3	3	3	0.0120	0.0096	0.0	110.4000	110.1000	109.5000

TORSION

EXPRESSION: ET=BARRIER HEIGHT*(1.0+SIGN*COS(FOLD*W))

"RANGE" ALLOWS CALCULATION OF TORSIONAL ENERGY ONLY WHEN TORSION ANGLE IS WITHIN THE SPECIFIED RANGE
"W" IS THE TORSION ANGLE

TYPE1	TYPE2	TYPE3	TYPE4	BARRIER HT	SIGN	FOLD	RANGE(+-)
1	2	2	1	6.2500	-1.0	2.0	0.0
1	2	2	3	6.2500	-1.0	2.0	0.0
3	2	2	3	6.2500	-1.0	2.0	0.0
1	2	3	1	0.1367	1.0	3.0	0.0
1	2	3	2	0.1367	1.0	3.0	0.0
1	2	3	3	0.1367	1.0	3.0	0.0
2	2	3	1	0.0629	-1.0	3.0	0.0
2	2	3	2	0.0629	-1.0	3.0	0.0
2	2	3	3	0.0629	-1.0	3.0	0.0
3	2	3	1	0.0629	1.0	3.0	0.0
3	2	3	2	0.0629	1.0	3.0	0.0
3	2	3	3	0.0629	1.0	3.0	0.0
1	3	3	1	0.1100	1.0	3.0	0.0
1	3	3	2	0.1100	1.0	3.0	0.0
1	3	3	3	0.1100	1.0	3.0	0.0
2	3	3	2	0.0200	1.0	3.0	0.0
2	3	3	3	0.0629	1.0	3.0	0.0
3	3	3	3	0.0629	1.0	3.0	0.0

OUT OF PLANE BENDING

EXPRESSION: EO=OP-BENDK*(180.0-CHI)**2

WHERE "CHI" IS THE IMPROPER TORSION ANGLE DEFINED BY WARSHEL,LEVITT,AND LIFSON (J.MOL.SPECTROSCOPY,1970,33,84)

TYPE1	TYPE2	TYPE3	TYPE4	OP-BENDK
3	2	2	1	0.0020

APPENDIX B

FFII ALKANE/ALKENE FORCE FIELD (ALLINGER BASED)

ATOM KEY

1 = C(SP)**2, 2 = C(SP)**3, 3 = BR, 4 = H,

FORCE CONSTANTS ARE IN KCAL/MOLE/ANGSTROM**2 OR IN KCAL/MOLE/DEGREE**2
ENERGIES ARE IN KCAL/MOLE

BOND STRETCHING

EXPRESSION: EB=STRETCHK1*(LENGTH-REF.LENGTH)**2

TYPE1	TYPE2	STRETCHK1	REF.LENGTH
1	1	690.8640	1.3320
1	2	316.6460	1.4960
1	4	331.0390	1.0900
2	2	316.6460	1.5300
2	3	179.7200	1.9300
2	4	331.0000	1.0940

VAN DER WAALS INTERACTIONS

EXPRESSION: EV=((-2.25/(ALPHA**6))*EPSILON)+(828000*EXP(-ALPHA/0.0736)*EPSILON)

ALPHA=DIST(1-2)/(RSTAR1+RSTAR2)

TYPE1	TYPE2	RSTAR1	RSTAR2	EPSILON
1	1	1.8500	1.8500	0.0330
1	2	1.8500	1.5500	0.0620
1	3	1.8500	1.9500	0.0440
1	4	1.8500	1.4500	0.0440
2	2	1.5500	1.5500	0.1160
2	3	1.5500	1.9500	0.2460
2	4	1.5500	1.4500	0.0840
3	3	1.9500	1.9500	0.5220
3	4	1.9500	1.4500	0.1770
4	4	1.4500	1.4500	0.0600

ANGLE BENDING

EXPRESSION: EA=BENDK1*(ANGLE-REF.ANGLE"N")**2

"N" REFERS TO DEGREE OF NON-HYDROGEN SUBSTITUTION ON THE CENTRAL ATOM OF THE ANGLE CONCERNED. ANGLES ARE IN DEGREES

TYPE1	TYPE2	TYPE3	BENDK1	REF.ANG1	REF.ANG2	REF.ANG3	REF.ANG4
1	1	2	0.0088	0.0	122.2000	0.0	0.0
1	1	4	0.0053	0.0	119.9000	0.0	0.0
2	1	4	0.0053	0.0	117.9000	0.0	0.0
1	2	2	0.0088	0.0	110.2000	110.6000	0.0
1	2	3	0.0088	0.0	0.0	110.0000	0.0
1	2	4	0.0053	0.0	112.8000	108.4000	0.0
2	2	2	0.0088	0.0	110.2000	110.6000	109.5000
2	2	3	0.0088	0.0	110.0000	110.0000	109.5000
2	2	4	0.0053	107.8000	112.8000	108.4000	0.0
3	2	4	0.0053	0.0	109.0000	109.0000	0.0
4	2	4	0.0044	111.2000	108.5000	0.0	0.0

TORSION

EXPRESSION: ET=BARRIER HEIGHT*(1.0+SIGN*COS(FOLD*W))

"RANGE" ALLOWS CALCULATION OF TORSIONAL ENERGY ONLY WHEN TORSION ANGLE IS WITHIN THE SPECIFIED RANGE
"W" IS THE TORSION ANGLE

TYPE1	TYPE2	TYPE3	TYPE4	BARRIER HT	SIGN	FOLD	RANGE(+-)
2	1	1	2	6.7700	-1.0	2.0	0.0
2	1	1	4	6.7700	-1.0	2.0	0.0
4	1	1	4	6.7700	-1.0	2.0	0.0
1	1	2	2	0.1541	-1.0	3.0	0.0
1	1	2	3	0.1541	-1.0	3.0	0.0
1	1	2	4	0.1541	-1.0	3.0	0.0
4	1	2	2	0.1541	1.0	3.0	0.0
4	1	2	3	0.1541	1.0	3.0	0.0
4	1	2	4	0.1541	1.0	3.0	0.0
1	2	2	1	0.1000	1.0	3.0	0.0
1	2	2	2	0.1000	1.0	3.0	0.0
1	2	2	3	0.1000	1.0	3.0	0.0
1	2	2	4	0.1000	1.0	3.0	0.0
2	2	2	4	0.1000	1.0	3.0	0.0
3	2	2	4	0.1000	1.0	3.0	0.0
4	2	2	4	0.1000	1.0	3.0	0.0

OUT OF PLANE BENDING

EXPRESSION: EO=OP-BENDK*(180.0-CHI)**2

WHERE "CHI" IS THE IMPROPER TORSION ANGLE DEFINED BY WARSHEL,LEVITT,AND LIFSON (J.MOL.SPECTROSCOPY,1970,33,84)

TYPE1	TYPE2	TYPE3	TYPE4	OP-BENDK
3	2	2	1	0.0035

APPENDIX C

FFIII SESQUITERPENE FORCE FIELD

ATOM KEY

1 = C(SP)**2, 2 = C(=O) , 3 = C(SP)**3, 4 = O(=C) , 5 = -O- ,

6 = H ,

FORCE CONSTANTS ARE IN KCAL/MOLE/ANGSTROM**2 OR IN KCAL/MOLE/DEGREE**2
ENERGIES ARE IN KCAL/MOLE

BOND STRETCHING

EXPRESSION: EB=STRETCHK1*(LENGTH-REF.LENGTH)**2

TYPE1	TYPE2	STRETCHK1	REF.LENGTH
1	1	690.8640	1.3320
1	2	316.6460	1.4800
1	3	316.6460	1.4960
1	6	331.0390	1.0900
2	3	316.6460	1.4960
2	4	777.2220	1.2100
2	5	474.9690	1.3340
3	3	316.6460	1.5300
3	5	309.4500	1.4700
3	6	331.0390	1.0940
5	6	503.7500	0.9520

VAN DER WAALS INTERACTIONS

EXPRESSION: EV=((-2.25/(ALPHA**6))*EPSILON)+(828000*EXP(-ALPHA/0.0736)*EPSILON)

ALPHA=DIST(1-2)/(RSTAR1+RSTAR2)

TYPE1	TYPE2	RSTAR1	RSTAR2	EPSILON
1	1	1.8500	1.8500	0.0330
1	2	1.8500	1.8500	0.0330
1	3	1.8500	1.5500	0.0620
1	4	1.8500	1.5400	0.0480
1	5	1.8500	1.5400	0.0480
1	6	1.8500	1.4500	0.0440
2	3	1.8500	1.5500	0.0620
2	5	1.8500	1.5400	0.0480
2	6	1.8500	1.4500	0.0440
3	3	1.5500	1.5500	0.1160
3	4	1.5500	1.5400	0.0900
3	5	1.5500	1.5400	0.0900
3	6	1.5500	1.4500	0.0840
4	5	1.5400	1.5400	0.0700
4	6	1.5400	1.4500	0.0650
5	5	1.5400	1.5400	0.0700
5	6	1.5400	1.4500	0.0650
6	6	1.4500	1.4500	0.0600

ANGLE BENDING

EXPRESSION: EA=BENDK1*(ANGLE-REF.ANGLE"N")**2

"N" REFERS TO DEGREE OF NON-HYDROGEN SUBSTITUTION ON THE CENTRAL ATOM OF THE ANGLE CONCERNED. ANGLES ARE IN DEGREES

TYPE1	TYPE2	TYPE3	BENDK1	REF.ANG1	REF.ANG2	REF.ANG3	REF.ANG4
1	1	2	0.0088	0.0	122.2000	121.7000	0.0
1	1	3	0.0088	0.0	122.2000	121.7000	0.0
1	1	6	0.0053	118.9000	119.9000	0.0	0.0
2	1	3	0.0088	0.0	0.0	116.6000	0.0
2	1	6	0.0053	0.0	117.9000	0.0	0.0
3	1	3	0.0088	0.0	0.0	116.6000	0.0
3	1	6	0.0053	0.0	117.9000	0.0	0.0
6	1	6	0.0044	122.2000	0.0	0.0	0.0
1	2	1	0.0088	0.0	0.0	115.6000	0.0
1	2	4	0.0125	0.0	122.2000	122.2000	0.0
1	2	5	0.0123	0.0	0.0	115.6000	0.0
3	2	4	0.0125	0.0	124.4000	124.4000	0.0
3	2	5	0.0123	0.0	0.0	115.6000	0.0
4	2	5	0.0156	0.0	0.0	120.0000	0.0
1	3	1	0.0088	0.0	110.2000	110.6000	109.5000
1	3	3	0.0088	0.0	110.2000	110.6000	109.5000
1	3	5	0.0110	0.0	110.2000	110.6000	109.5000
1	3	6	0.0053	107.8000	112.8000	108.4000	0.0
2	3	3	0.0088	0.0	110.2000	110.6000	109.5000
2	3	6	0.0053	107.8000	108.5000	108.4000	0.0
3	3	3	0.0088	0.0	110.2000	110.6000	109.5000
3	3	5	0.0110	0.0	110.2000	110.6000	109.5000
3	3	6	0.0053	107.8000	112.8000	108.4000	0.0
5	3	6	0.0097	107.8000	112.8000	108.4000	0.0
6	3	6	0.0044	111.2000	108.5000	0.0	0.0
2	5	3	0.0221	0.0	114.8000	0.0	0.0
3	5	6	0.0167	95.2000	0.0	0.0	0.0

TORSION

EXPRESSION: ET=BARRIER HEIGHT*(1.0+SIGN*COS(FOLD*W))

"RANGE" ALLOWS CALCULATION OF TORSIONAL ENERGY ONLY WHEN TORSION ANGLE IS WITHIN THE SPECIFIED RANGE
"W" IS THE TORSION ANGLE

TYPE1	TYPE2	TYPE3	TYPE4	BARRIER HT	SIGN	FOLD	RANGE(+-)
2	1	1	3	6.7700	-1.0	2.0	0.0
3	1	1	3	6.7700	-1.0	2.0	0.0
2	1	1	6	6.7700	-1.0	2.0	0.0
3	1	1	6	6.7700	-1.0	2.0	0.0
6	1	1	6	6.7700	-1.0	2.0	0.0
1	1	2	1	1.3000	-1.0	2.0	0.0
1	1	2	4	1.3000	-1.0	2.0	0.0
1	1	2	5	1.3000	-1.0	2.0	0.0
3	1	2	1	1.3000	-1.0	2.0	0.0
3	1	2	4	1.3000	-1.0	2.0	0.0
3	1	2	5	1.3000	-1.0	2.0	0.0
6	1	2	1	1.3000	-1.0	2.0	0.0
6	1	2	4	1.3000	-1.0	2.0	0.0
1	1	3	1	0.1800	-1.0	3.0	0.0
1	1	3	3	0.1800	-1.0	3.0	0.0
1	1	3	5	0.1800	-1.0	3.0	0.0
1	1	3	6	0.1800	-1.0	3.0	0.0
2	1	3	3	0.1800	1.0	3.0	0.0
2	1	3	6	0.1800	1.0	3.0	0.0
3	1	3	1	0.1800	1.0	3.0	0.0
3	1	3	3	0.1800	1.0	3.0	0.0
3	1	3	5	0.1800	1.0	3.0	0.0
3	1	3	6	0.1800	1.0	3.0	0.0
6	1	3	1	0.1600	1.0	3.0	0.0

TORSION (CONTINUED)

TYPE1	TYPE2	TYPE3	TYPE4	BARRIER HT	SIGN	FOLD	RANGE(+-)
6	1	3	3	0.1600	1.0	3.0	0.0
6	1	3	5	0.1800	1.0	3.0	0.0
6	1	3	6	0.1800	1.0	3.0	0.0
4	2	3	3	-0.7450	1.0	3.0	60.0
4	2	3	6	-0.3050	1.0	3.0	60.0
5	2	3	3	0.0450	1.0	3.0	0.0
5	2	3	6	-0.0200	1.0	3.0	0.0
1	2	5	3	5.9210	-1.0	2.0	0.0
3	2	5	3	5.9210	-1.0	2.0	0.0
4	2	5	3	5.9210	-1.0	2.0	0.0
1	3	3	1	0.0830	1.0	3.0	0.0
1	3	3	3	0.0830	1.0	3.0	0.0
1	3	3	5	0.0830	1.0	3.0	0.0
1	3	3	6	0.0830	1.0	3.0	0.0
2	3	3	3	0.0830	1.0	3.0	0.0
3	3	3	3	0.0830	1.0	3.0	0.0
5	3	3	3	0.0830	1.0	3.0	0.0
2	3	3	6	0.0830	1.0	3.0	0.0
3	3	3	6	0.0830	1.0	3.0	0.0
5	3	3	6	0.0830	1.0	3.0	0.0
6	3	3	6	0.0830	1.0	3.0	0.0
1	3	5	2	0.2000	1.0	3.0	0.0
1	3	5	6	0.2000	1.0	3.0	0.0
3	3	5	2	0.2000	1.0	3.0	0.0
3	3	5	6	0.2000	1.0	3.0	0.0
6	3	5	2	0.2000	1.0	3.0	0.0
6	3	5	6	0.2000	1.0	3.0	0.0

OUT OF PLANE BENDING

EXPRESSION: EO=OP-BENDK*(180.0-CHI)**2

WHERE "CHI" IS THE IMPROPER TORSION ANGLE DEFINED BY WARSHEL,LEVITT,AND LIFSON (J.MOL.SPECTROSCOPY,1970,33,84)

TYPE1	TYPE2	TYPE3	TYPE4	OP-BENDK
3	1	1	6	0.0035
3	1	1	3	0.0035
5	2	1	4	0.0092
5	2	3	4	0.0092